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DICTIONARY FILE UPDATES:  19 FEB 2007  HIGHEST RN 921921-74-6

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http://www.cas.org/ONLINE/UG/regprops.html

=> file caplus
FILE 'CAPLUS' ENTERED AT 09:42:26 ON 20 FEB 2007
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FILE COVERS 1907 - 20 Feb 2007  VOL 146 ISS 9
FILE LAST UPDATED: 19 Feb 2007  (20070219/ED)

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http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

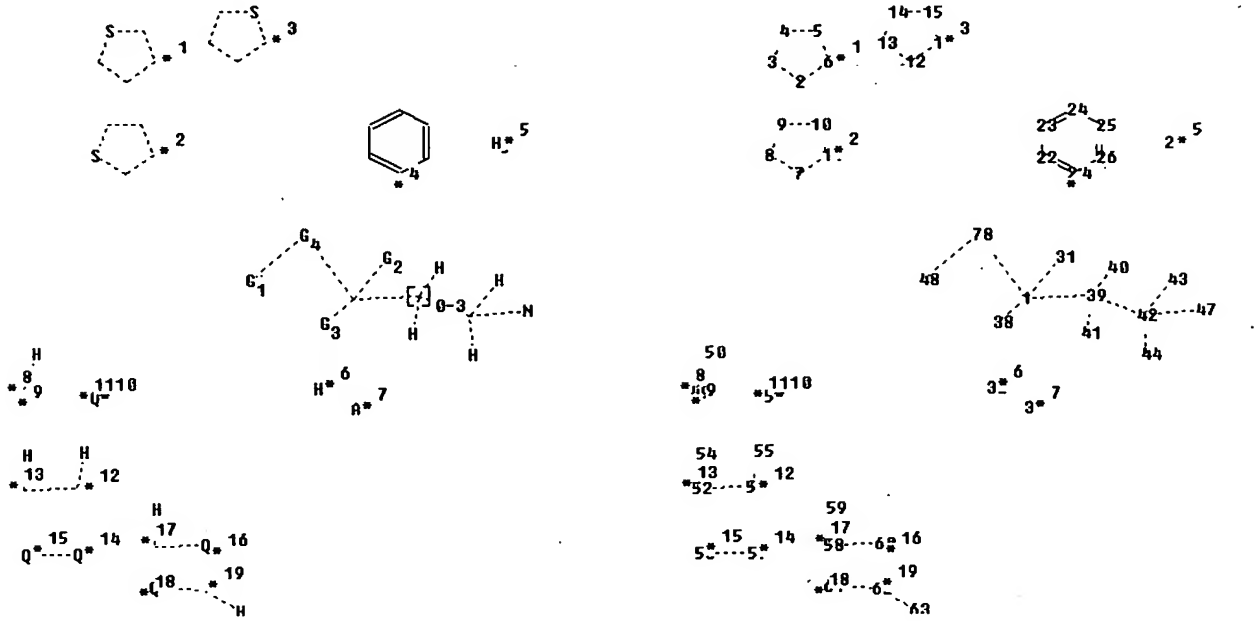
=> d stat que L51
L49          39 SEA FILE=CAPLUS ABB=ON  PLU=ON  METE A?/AU
L50          49 SEA FILE=CAPLUS ABB=ON  PLU=ON  WALTERS I?/AU
L51           5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L49 AND L50

=> d stat que L52
```

L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:
Uploading L3.str



chain nodes :
27 31 32 33 38 40 41 43 44 50 54 55 59 63
ring nodes :
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 21 22 23 24 25 26
ring/chain nodes :
1 39 42 47 48 49 51 52 53 56 57 58 60 61 62 78
chain bonds :
1-31 1-38 39-40 39-41 42-43 42-44 49-50 52-54 53-55 58-59 62-63
ring/chain bonds :
1-39 1-78 39-42 42-47 48-78 52-53 56-57 58-60 61-62
ring bonds :
2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13 12-16 13-14 14-15
15-16 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
1-39 1-31 1-38 1-78 2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13
12-16 13-14 14-15 15-16 39-40 39-41 39-42 42-43 42-44 42-47 48-78 49-50
52-53 52-54
53-55 56-57 58-59 58-60 61-62 62-63
normalized bonds :
21-22 21-26 22-23 23-24 24-25 25-26

G1:[*1],[*2],[*3]

G2:[*4],[*5]

G3:[*6],[*7]

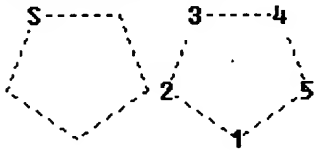
G4:[*8-*9],[*10-*11],[*12-*13],[*14-*15],[*16-*17],[*18-*19]

Connectivity :
33:1 E exact RC ring/chain
Match level :
1:CLASS 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 21:Atom 22:Atom 23:Atom
24:Atom 25:Atom
26:Atom 27:Atom 31:CLASS 32:CLASS 33:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS 52:CLASS
53:CLASS 54:CLASS
55:CLASS 56:CLASS 57:CLASS 58:CLASS 59:CLASS 60:CLASS 61:CLASS 62:CLASS
63:CLASS 78:CLASS

Generic attributes :
27:
Saturation : Unsaturated

L4 STR

Structure attributes must be viewed using STN Express query preparation:
Uploading L4.str



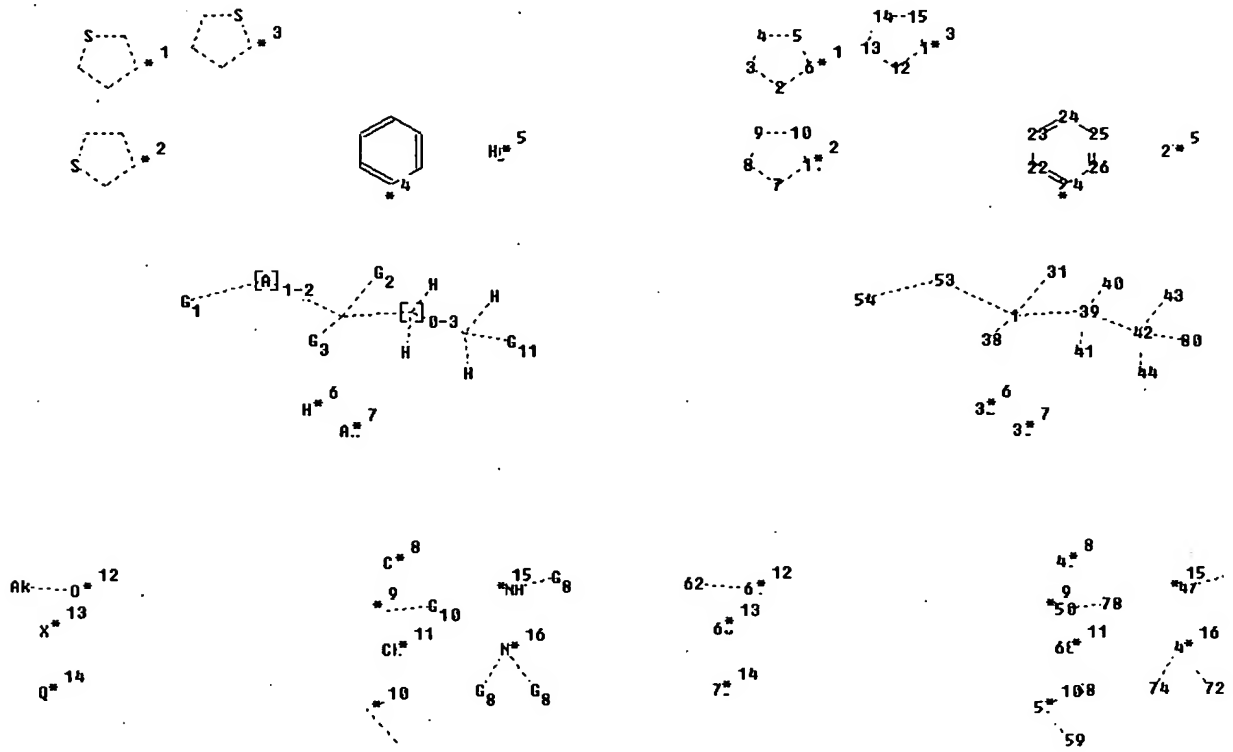
ring nodes :
1 2 3 4 5
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom

L5 2142 SEA FILE=REGISTRY SSS FUL L3 AND L4
L37 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:
Uploading L37.str



chain nodes :
27 31 32 33 38 40 41 43 44 47 48 50 57 61 62 63 68 71 72 74 78

ring nodes :
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 21 22 23 24 25 26 49 75

ring/chain nodes :
1 39 42 53 54 58 59 80
chain bonds :
1-31 1-38 39-40 39-41 42-43 42-44 47-71 48-72 48-74 50-78 57-58 57-59
61-62
ring/chain bonds :
1-39 1-53 39-42 42-80 53-54
ring bonds :
2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13 12-16 13-14 14-15
15-16 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
1-39 1-31 1-38 1-53 2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13
12-16 13-14 14-15 15-16 39-40 39-41 39-42 42-43 42-44 42-80 47-71 48-72
48-74 50-78
53-54 57-58 57-59 61-62
normalized bonds :
21-22 21-26 22-23 23-24 24-25 25-26

G1:[*1],[*2],[*3]

G2:[*4],[*5]

G3:[*6],[*7]

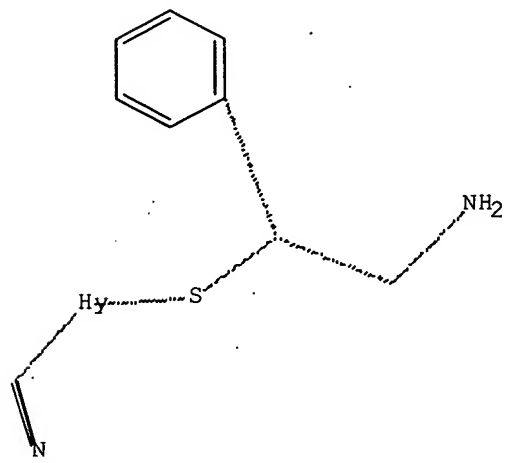
G8:[*8],[*9],[*10],[*11]

G10:[*12],[*13],[*14]

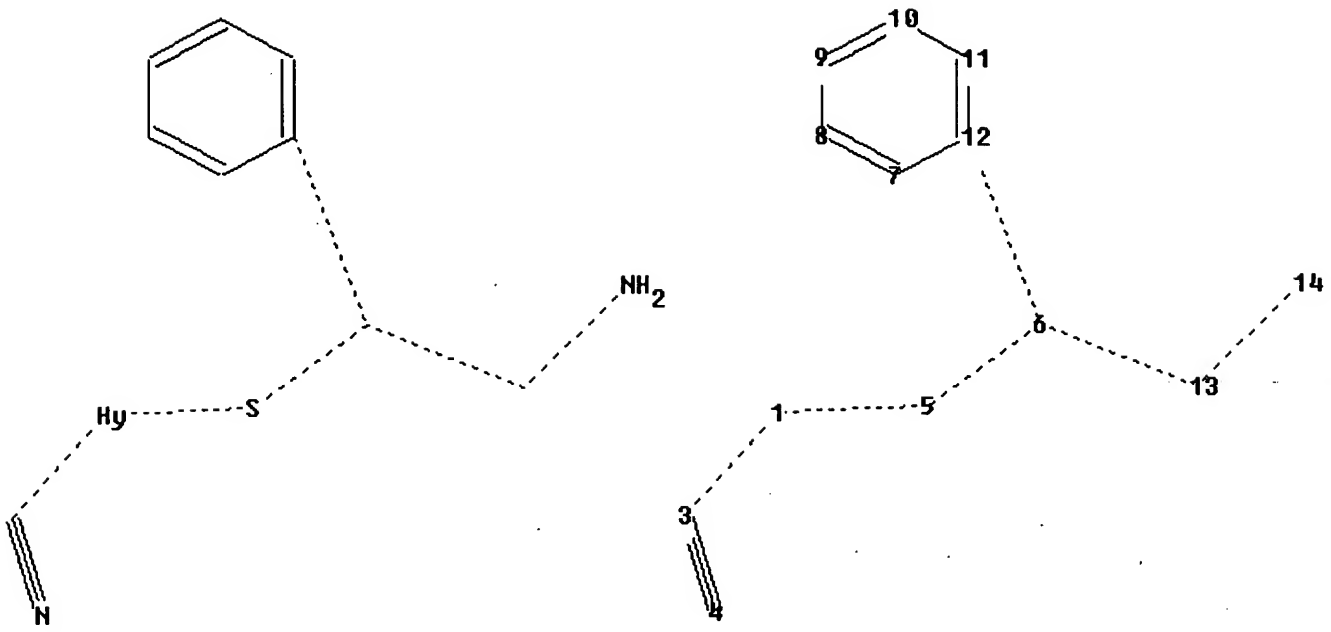
G11:NH2,[*15],[*16]

Connectivity :
33:1 E exact RC ring/chain
Match level :
1:CLASS 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 21:Atom 22:Atom 23:Atom
24:Atom 25:Atom
26:Atom 27:Atom 31:CLASS 32:CLASS 33:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 47:CLASS 48:CLASS 49:Atom 50:CLASS 53:CLASS 54:CLASS
57:CLASS 58:CLASS
59:CLASS 61:CLASS 62:CLASS 63:CLASS 68:CLASS 71:CLASS 72:CLASS 74:CLASS
75:Atom 78:CLASS
80:CLASS
Generic attributes :
27:
Saturation : Unsaturated

L39 31 SEA FILE=REGISTRY SUB=L5 SSS FUL L37
L41 16 SEA FILE=CAPLUS ABB=ON PLU=ON L39
L42 STR



Structure attributes must be viewed using STN Express query preparation:
Uploading L42.str



chain nodes :
1 3 4 5 6 13 14
ring nodes :
7 8 9 10 11 12
chain bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

Match level :
1:Atom 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom
12:Atom 13:CLASS 14:CLASS
Generic attributes :
1:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 1: Limited
C,C4
S,S1

L44 2 SEA FILE=REGISTRY SSS FUL L42
L45 1 SEA FILE=CAPLUS ABB=ON PLU=ON L44

```
L49          39 SEA FILE=CAPLUS ABB=ON  PLU=ON  METE A?/AU
L50          49 SEA FILE=CAPLUS ABB=ON  PLU=ON  WALTERS I?/AU
L52           2 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L41 OR L45) AND (L49 OR L50)


=> s L51-L52
L53          6 (L51 OR L52)

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=> s L51
L54          6 L51

=> dup rem L53 L54
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PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L54
L55           6 DUP REM L53 L54 (6 DUPLICATES REMOVED)
                ANSWERS '1-6' FROM FILE CAPLUS

=> d ibib abs hitstr L55 1-6

L55  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2007 ACS on STN  DUPLICATE 1
ACCESSION NUMBER:         2004:498557  CAPLUS  Full-text
DOCUMENT NUMBER:          141:206886
TITLE:                    Synthesis and evaluation of substrate-mimicking
                          cytosolic phospholipase A2 inhibitors--reducing the
                          lipophilicity of the arachidonyl chain isostere
AUTHOR(S):                Walters, Iain; Bennion, Colin; Connolly,
                          Stephen; Croshaw, Pamela J.; Hardy, Kim; Hartopp,
                          Paul; Jackson, Clive G.; King, Sarah J.; Lawrence,
                          Louise; Mete, Antonio; Murray, David;
                          Robinson, David H.; Stein, Linda; Wells, Edward;
                          Withnall, W. John
CORPORATE SOURCE:         R & D Charnwood, Departments of Medicinal Chemistry,
                          Molecular Biology, and Discovery BioScience,
                          AstraZeneca, Leicestershire, LE11 5RH, UK
SOURCE:                   Bioorganic & Medicinal Chemistry Letters (2004),
                          14(14), 3645-3649
                          CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER:                Elsevier Science B.V.
DOCUMENT TYPE:            Journal
```

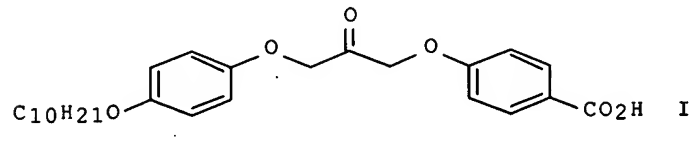
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:206886

AB The high lipophilicity of a series of cytosolic phospholipase A2 inhibitors has been reduced by the modification of a decyloxyphenyl chain designed to mimic the arachidonyl group of the natural substrate. These changes have resulted in an improvement in the whole cell potency of the inhibitors.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:106165 CAPLUS Full-text
DOCUMENT NUMBER: 136:294618
TITLE: Design and Synthesis of a Novel and Potent Series of Inhibitors of Cytosolic Phospholipase A2 Based on a 1,3-Disubstituted Propan-2-one Skeleton
AUTHOR(S): Connolly, Stephen; Bennion, Colin; Botterell, Sarah; Croshaw, Pamela J.; Hallam, Catherine; Hardy, Kim; Hartopp, Paul; Jackson, Clive G.; King, Sarah J.; Lawrence, Louise; ***Mete, Antonio***; Murray, David; Robinson, David H.; Smith, Gillian M.; Stein, Linda; ***Walters, Iain***; Wells, Edward; Withnall, W. John
CORPORATE SOURCE: Departments of Medicinal Chemistry Molecular Biology and Discovery BioScience, AstraZeneca R&D Charnwood, Loughborough Leicestershire, LE11 5RH, UK
SOURCE: Journal of Medicinal Chemistry (2002), 45(6), 1348-1362
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:294618
GI



I

AB Using knowledge of the substrate specificity of cPLA2 (phospholipases A2), a novel series of inhibitors of this enzyme were designed based upon a three point model of inhibitor binding to the enzyme active site comprising a lipophilic anchor, an electrophilic serine trap, and an acidic binding moiety. The resulting 1,3-diheteroatom-substituted propan-2-ones were evaluated as inhibitors of cPLA2 in both aggregated bilayer and soluble substrate assays. Systematic variation of the lipophilic, electrophilic, and acidic groups revealed a well-defined structure-activity relationship against the enzyme. Optimization of each group led to AR-C70484XX (I), which contains a decyloxy lipophilic side chain, a 1,3-diaryloxypropan-2-one moiety as a unique serine trap, and a benzoic acid as the acidic binding group. I is among the most potent in vitro inhibitors of cPLA2 described to date being more than 20-fold more active against the isolated enzyme (IC50 = 0.03 μM) than the standard cPLA2 inhibitor, arachidonyl trifluoromethyl ketone (II), and also greater

than 10-fold more active than II against the cellular production of arachidonic acid by HL60 cells (IC50 = 2.8 μM).

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1080878 CAPLUS Full-text

DOCUMENT NUMBER: 142:56354

TITLE: Preparation of N-pyrazinyl arylsulfonamides that modulate chemokine (CCR4) receptor activity

INVENTOR(S): Harrison, Richard; ***Mete, Antonio***; Teobald, Barry; ***Walters, Iain***

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108692	A1	20041216	WO 2004-SE850	20040602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1633729	A1	20060315	EP 2004-748975	20040602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006526618	T	20061124	JP 2006-508570	20040602
US 2006122195	A1	20060608	US 2005-559312	20051202
PRIORITY APPLN. INFO.:			SE 2003-1653 A	20030605
			WO 2004-SE850 W	20040602

OTHER SOURCE(S): CASREACT 142:56354; MARPAT 142:56354

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar1 = (un)substituted Ph, thienyl; R4 = alkoxy; one of R5, R6 = XCH2alkyl and the other is H, halo, amino, etc.; X = amino, O, SO0-2, bond] are prepared For instance, II is prepared in 5 steps from 3,5-dichloro-2-pyrazineamine, 2,3-dichlorobenzenesulfonyl chloride and D-cysteine Me ester. Selected example compds. exhibited pIC50 of 6.2 and 6.4 for the human recombinant CCR4 receptor. I are useful for the treatment of inflammation.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

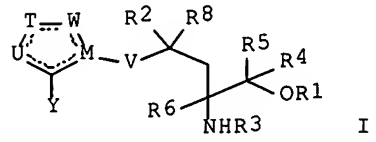
L55 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:80678 CAPLUS Full-text

DOCUMENT NUMBER: 140:145993
TITLE: Preparation of aminohydroxyalkylthiothiophenecarbonitriles as nitric oxide synthase (NOS) inhibitors.
INVENTOR(S): ***Mete, Antonio; Walters, Iain***
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009580	A1	20040129	WO 2003-SE1215	20030715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003245230	A1	20040209	AU 2003-245230	20030715
EP 1539731	A1	20050615	EP 2003-738863	20030715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006504655	T	20060209	JP 2004-522890	20030715
US 2005203172	A1	20050915	US 2005-521727	20050118
PRIORITY APPLN. INFO.:			SE 2002-2279 A	20020719
			WO 2003-SE1215 W	20030715

OTHER SOURCE(S): MARPAT 140:145993
GI



I

AB Title compds. [I; Y = (fluoro)alkyl, (fluoro)alkoxy, halo, CN, C:CH, NO2, CH2OH, CHO, Ac, NH2, NHCHO, NHCOCH3, NHSO2Me; T, U, W = CX, N, NR13, O, SOm; m = 0-2; X = H, (fluoro)alkyl, (fluoro)alkoxy, halo, OH, SH, CN, C:CH, N(R14)2, NO2, CH2OH, CHO, Ac, NHCHO; V = NR7, O, CH2, SOn, CH2O, CH2NR7, CH2SOn, CH2CH2, CH:CH; n = 0-2; M = C, N; R1, R8 = H, Me.; R2 = alkyl, alkenyl, alkynyl, cycloalkyl, 4-8 membered saturated heterocyclyl incorporating 1 O, S, N; any of said groups being optionally further substituted by alkyl, alkoxy, alkylthio, cycloalkyl, halo, (substituted) Ph; or R2 = (substituted) Ph, 5-6 membered heteroaryl containing 1-3 O, S, N; R3 = H, (substituted) alkyl; cycloalkyl; R4-R7, R9-R12, R14 = H, alkyl; R13 = H, alkyl, CHO, Ac, SO2CH3, CF3], were prepared Thus, 1,1-dimethylethyl (4S)-4-((2R)-2-mercapto-2-

phenylethyl)-2,2-dimethyl-3- oxazolidinecarboxylate (preparation given), 3-bromothiophene-2-carbonitrile, and NaH were stirred 24 h in DMF to give 1,1-dimethylethyl (4S)-4-[(2R)-2-[(2-cyano-3-thienyl)thio]-2-phenylethyl]-2,2-dimethyl-3- oxazolidinecarboxylate. The latter was stirred 2 h with 4M HCl in dioxane to give a residue which was treated with oxalic acid in Et2O to give 3-[[(1R,3S)-3-amino-4-hydroxy-1-phenylbutyl]thio]-2-thiophenecarbonitrile oxalate. I inhibited iNOS with IC50 <10 μM.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:80677 CAPLUS Full-text

DOCUMENT NUMBER: 140:128265

TITLE: Preparation of 3-[((1S)-2-amino-1-phenylethyl)thio]-5-methyl-2-thiophenecarbonitrile oxalate and related compounds as nitric oxide synthase inhibitors.

INVENTOR(S): ***Mete, Antonio; Walters, Iain***

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.

SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

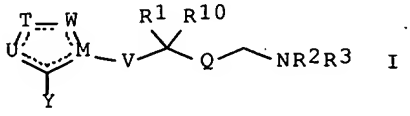
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004009579	A1	20040129	WO 2003-SE1214	20030715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003251259	A1	20040209	AU 2003-251259	20030715
EP 1539732	A1	20050615	EP 2003-765417	20030715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005537281	T	20051208	JP 2004-522889	20030715
US 2006019999	A1	20060126	US 2005-521728	20050118
PRIORITY APPLN. INFO.:			SE 2002-2280 A	20020719
			WO 2003-SE1214 W	20030715

OTHER SOURCE(S): MARPAT 140:128265

GI



I

AB Title compds. [I; Y = (F-substituted) alkyl, alkoxy, halo, CN, C:CH, NO2, CH2OH, CHO, Ac, NH2, NHCHO, NHAc, NHSO2Me; T, U, W = CX, N, NR9, O, S(O)m, ≥1 of T, U, W must = heteroatom and ≤1 of T, U and W may = NR9, O, SOm; m, n = 0-2; X = H, (F-substituted) alkyl, alkoxy, halo, OH, SH, CN, C:CH, N(R11)2, NO2, CH2OH, CHO, Ac, NHCHO; V = NR4, O, CH2, SOn, OCH2, CH2O, NR4CH2, CH2NR4, CH2SOn, SOnCH2, CH2CH2, CH:CH; M = C, and when M is bonded to a CH2 moiety in V, then M may = N; R10 = H, Me. Q = (CH2)p; p = 0-3; R1 = (substituted) Ph, 5-6 membered heteroaryl containing 1-3 O, S and N; R2, R3 = H, (substituted) alkyl, cycloalkyl; Z = CO, bond; R4, R11 = H, alkyl; R5-R8 = H, alkyl; R9 = H, alkyl, CHO, Ac, SO2Me, CF3], were prepared Thus, S-[(1S)-2-[[(1,1-dimethylethoxy)carbonyl]amino]-1- phenylethyl]benzenecarbothioate (preparation given) was stirred 2h with aqueous NH3 in MeOH; the residue was stirred with 3-bromo-5-methyl-2- thiophenecarbonitrile (preparation given) and Cs2CO3 in DMF for 24 h to give 1,1-dimethylethyl [(2S)-2-[(2-cyano-5-methyl-3-thienyl)thio]-2- phenylethyl]carbamate. The latter was stirred with 4M HCl in dioxane at 20° for 2 h and the residue was treated with oxalic acid in Et2O to give 3-[((1S)-2-amino-1-phenylethyl)thio]-5-methyl-2-thiophenecarbonitrile oxalate. The latter inhibited nitric oxide synthase with IC50 <100 μM.

IT ***651034-24-1P***

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aminophenylethylthiomethylthiophenecarbonitrile and related compds. as nitric oxide synthase inhibitors)

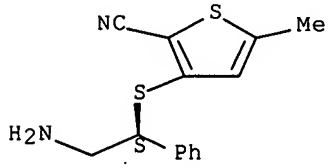
RN 651034-24-1 CAPLUS

CN 2-Thiophenecarbonitrile, 3-[[(1S)-2-amino-1-phenylethyl]thio]-5-methyl-, ethanedioate (9CI) (CA INDEX NAME)

CM 1

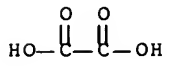
CRN 651034-23-0
CMF C14 H14 N2 S2

Absolute stereochemistry.



CM 2

CRN 144-62-7
CMF C2 H2 O4



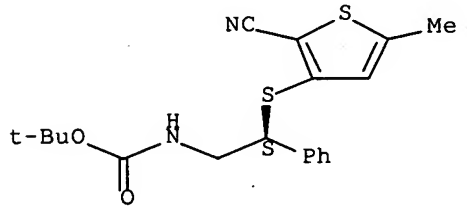
IT ***651034-45-6P***

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminophenylethylthiomethylthiophenecarbonitrile and related compds. as nitric oxide synthase inhibitors)

RN 651034-45-6 CAPLUS

CN Carbamic acid, [(2S)-2-[(2-cyano-5-methyl-3-thienyl)thio]-2-phenylethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L55 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:772637 CAPLUS Full-text

DOCUMENT NUMBER: 133:335251

TITLE: Preparation of 5,7-bicyclic amidine derivatives useful as nitric oxide synthase inhibitors

INVENTOR(S): Cheshire, David; Connolly, Stephen; Cox, David; Hamley, Peter; Luker, Timothy; ***Mete, Antonio***; Pimm, Austen; Stocks, Michael

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 93 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064904	A1	20001102	WO 2000-SE796	20000426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 1999-1530 A 19990428

OTHER SOURCE(S): MARPAT 133:335251

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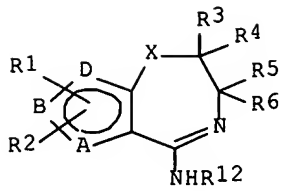


I

AB The title compds. I [A, B and D are independently selectev155d from C, N, O, and S, at least one of A, B and D being N, O or S, so as to form a 5-membered heterocyclic aromatic ring; X = CH2, NR7, O, SOm, etc.; R1, R2 = H, halo, alkyl, etc.; R3-R6 = H, alkyl, alkenyl, etc.; R12 = H, CO2R13], inhibitors of nitric oxide synthase, were prepared E.g., 2,3-dihydrothieno[2,3-f][1.4]thiazepin-5-ylamine hydrochloride was prepared

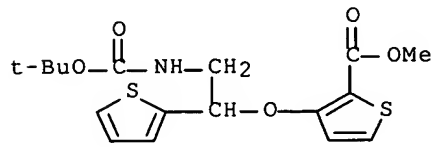
IT ***304021-24-7P***

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 5,7-bicyclic amidine derivs. useful as nitric oxide synthase inhibitors)

RN 304021-24-7 CAPLUS

CN 2-Thiophenecarboxylic acid, 3-[2-[[(1,1-dimethylethoxy)carbonyl]amino]-1-(2-thienyl)ethoxy]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STRUCTURE FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6
DICTIONARY FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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experimental property data in the original document. For information
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=> file caplus
FILE 'CAPLUS' ENTERED AT 09:44:54 ON 20 FEB 2007
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FILE COVERS 1907 - 20 Feb 2007 VOL 146 ISS 9
FILE LAST UPDATED: 19 Feb 2007 (20070219/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

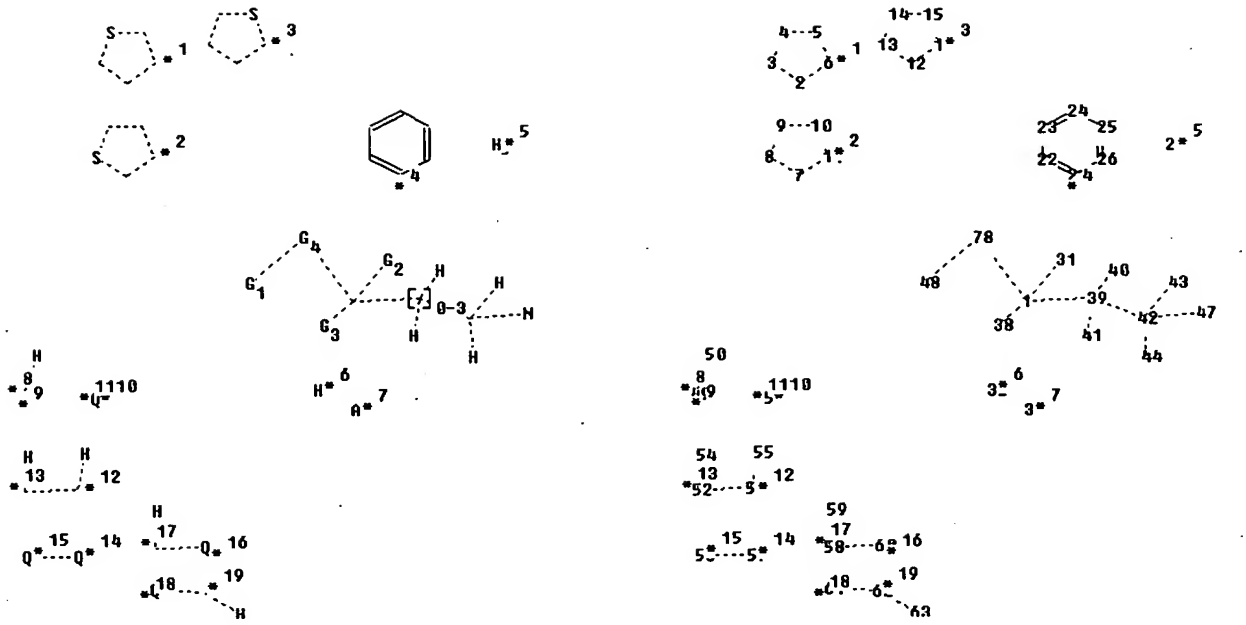
http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d stat que L41
L3 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:

Uploading L3.str



chain nodes :
27 31 32 33 38 40 41 43 44 50 54 55 59 63
ring nodes :
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 21 22 23 24 25 26
ring/chain nodes :
1 39 42 47 48 49 51 52 53 56 57 58 60 61 62 78
chain bonds :
1-31 1-38 39-40 39-41 42-43 42-44 49-50 52-54 53-55 58-59 62-63
ring/chain bonds :
1-39 1-78 39-42 42-47 48-78 52-53 56-57 58-60 61-62
ring bonds :
2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13 12-16 13-14 14-15
15-16 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
1-39 1-31 1-38 1-78 2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13
12-16 13-14 14-15 15-16 39-40 39-41 39-42 42-43 42-44 42-47 48-78 49-50
52-53 52-54
53-55 56-57 58-59 58-60 61-62 62-63
normalized bonds :
21-22 21-26 22-23 23-24 24-25 25-26

G1:[*1],[*2],[*3]

G2:[*4],[*5]

G3:[*6],[*7]

G4:[*8-*9],[*10-*11],[*12-*13],[*14-*15],[*16-*17],[*18-*19]

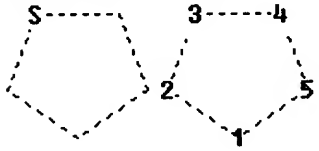
Connectivity :
33:1 E exact RC ring/chain

Match level :
1:CLASS 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 21:Atom 22:Atom 23:Atom
24:Atom 25:Atom
26:Atom 27:Atom 31:CLASS 32:CLASS 33:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS 52:CLASS
53:CLASS 54:CLASS
55:CLASS 56:CLASS 57:CLASS 58:CLASS 59:CLASS 60:CLASS 61:CLASS 62:CLASS
63:CLASS 78:CLASS

Generic attributes :
27:
Saturation : Unsaturated

L4 STR

Structure attributes must be viewed using STN Express query preparation:
Uploading L4.str



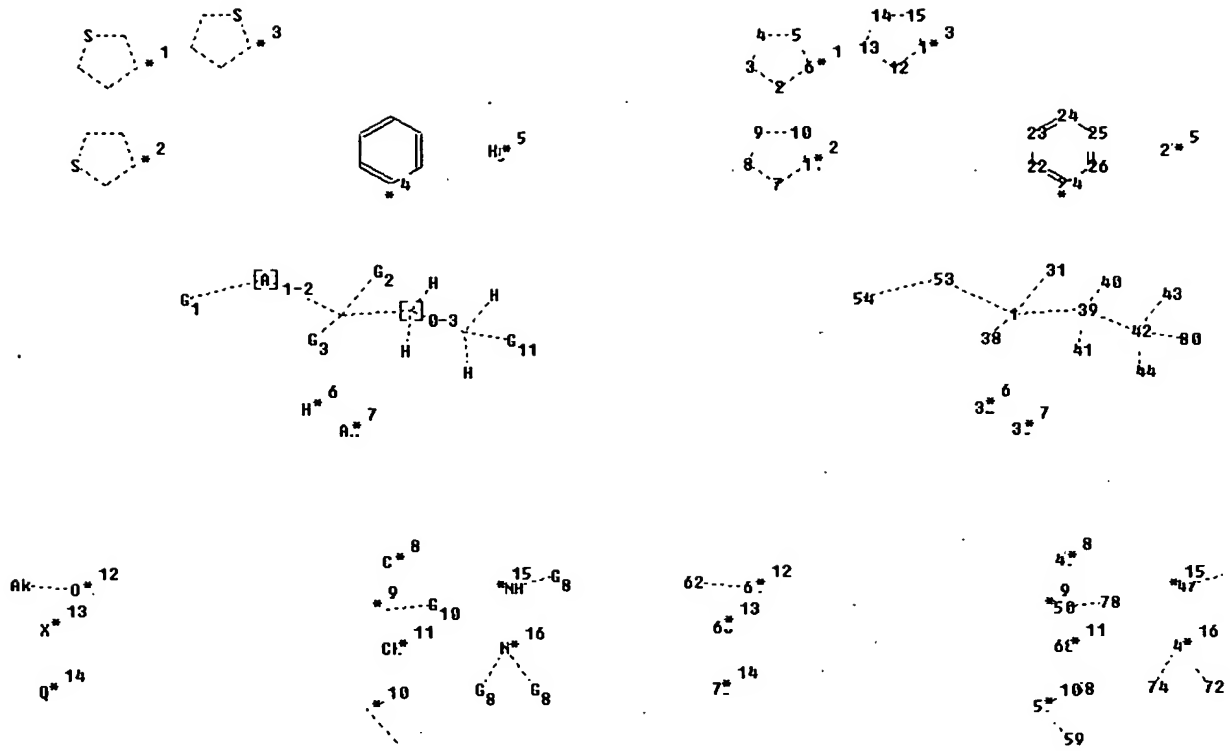
ring nodes :
1 2 3 4 5
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 2-3 3-4 4-5

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom

L5 2142 SEA FILE=REGISTRY SSS FUL L3 AND L4
L37 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:
Uploading L37.str



chain nodes :
27 31 32 33 38 40 41 43 44 47 48 50 57 61 62 63 68 71 72 74 78

ring nodes :
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 21 22 23 24 25 26 49 75

ring/chain nodes :
1 39 42 53 54 58 59 80
chain bonds :
1-31 1-38 39-40 39-41 42-43 42-44 47-71 48-72 48-74 50-78 57-58 57-59
61-62
ring/chain bonds :
1-39 1-53 39-42 42-80 53-54
ring bonds :
2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13 12-16 13-14 14-15
15-16 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
1-39 1-31 1-38 1-53 2-3 2-6 3-4 4-5 5-6 7-8 7-11 8-9 9-10 10-11 12-13
12-16 13-14 14-15 15-16 39-40 39-41 39-42 42-43 42-44 42-80 47-71 48-72
48-74 50-78
53-54 57-58 57-59 61-62
normalized bonds :
21-22 21-26 22-23 23-24 24-25 25-26

G1:[*1],[*2],[*3]

G2:[*4],[*5]

G3:[*6],[*7]

G8:[*8],[*9],[*10],[*11]

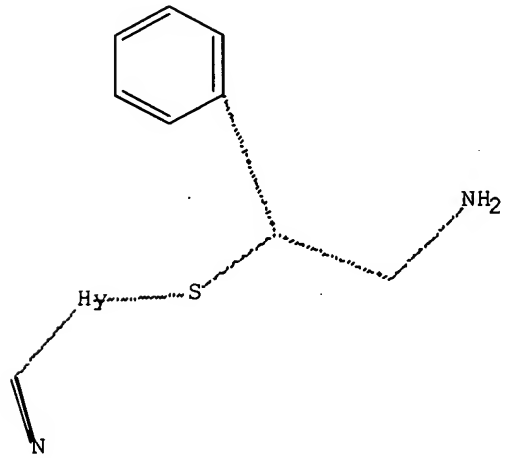
G10:[*12],[*13],[*14]

G11:NH2,[*15],[*16]

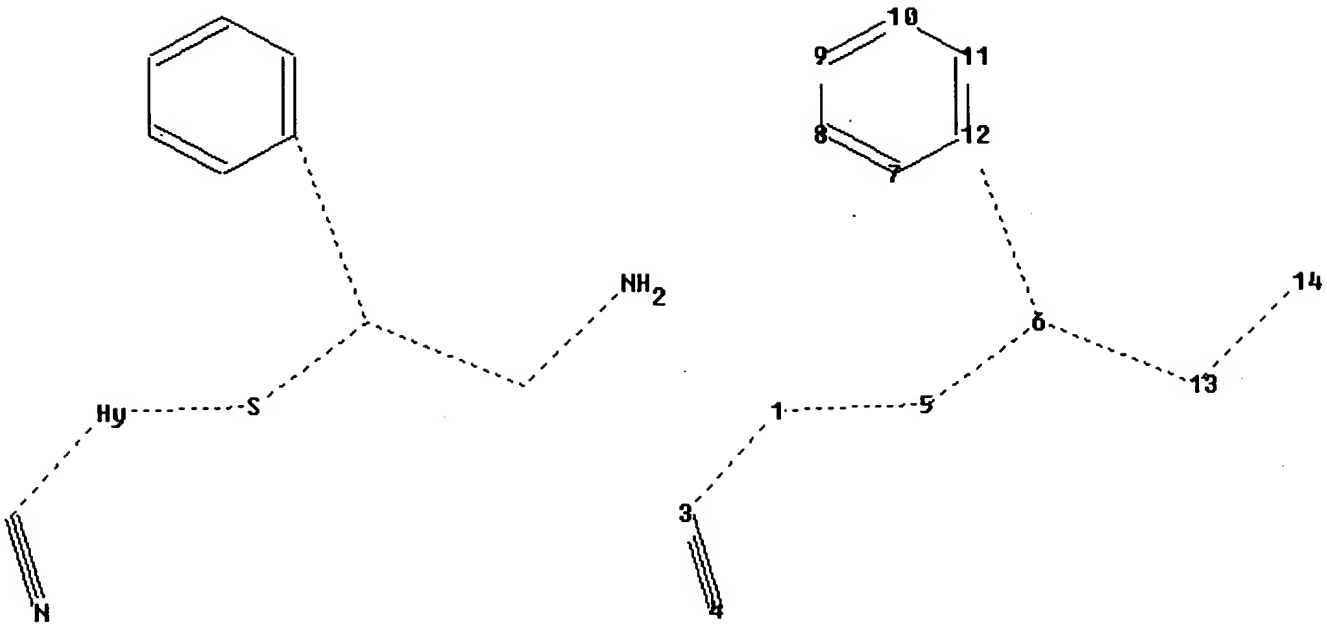
Connectivity :
33:1 E exact RC ring/chain
Match level :
1:CLASS 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 21:Atom 22:Atom 23:Atom
24:Atom 25:Atom
26:Atom 27:Atom 31:CLASS 32:CLASS 33:CLASS 38:CLASS 39:CLASS 40:CLASS
41:CLASS 42:CLASS
43:CLASS 44:CLASS 47:CLASS 48:CLASS 49:Atom 50:CLASS 53:CLASS 54:CLASS
57:CLASS 58:CLASS
59:CLASS 61:CLASS 62:CLASS 63:CLASS 68:CLASS 71:CLASS 72:CLASS 74:CLASS
75:Atom 78:CLASS
80:CLASS
Generic attributes :
27:
Saturation : Unsaturated

L39 31 SEA FILE=REGISTRY SUB=L5 SSS FUL L37
L41 16 SEA FILE=CAPLUS ABB=ON PLU=ON L39

=> d stat que L45
L42 STR



Structure attributes must be viewed using STN Express query preparation:
Uploading L42.str



chain nodes :
1 3 4 5 6 13 14
ring nodes :
7 8 9 10 11 12
chain bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

Match level :
1:Atom 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom
12:Atom 13:CLASS 14:CLASS
Generic attributes :
1:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 1: Limited
C,C4
S,S1

L44 2 SEA FILE=REGISTRY SSS FUL L42
L45 1 SEA FILE=CAPLUS ABB=ON PLU=ON L44

```
=> s (L41 or L45) not L53
L56         14 (L41 OR L45) NOT L53

=> file marpat
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FILE CONTENT: 1961-PRESENT VOL 146 ISS 7 (20070216/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US   2007004775 04 JAN 2007
DE 102005029574 28 DEC 2006
EP      1739181 03 JAN 2007
JP   2006351418 28 DEC 2006
WO   2007004364 11 JAN 2007
GB      2427193 20 DEC 2006
FR      2887681 29 DEC 2006
RU      2290406 27 DEC 2006
CA      2510093 16 DEC 2006

Expanded G-group definition display now available.

=> d stat que L48
L42             STR
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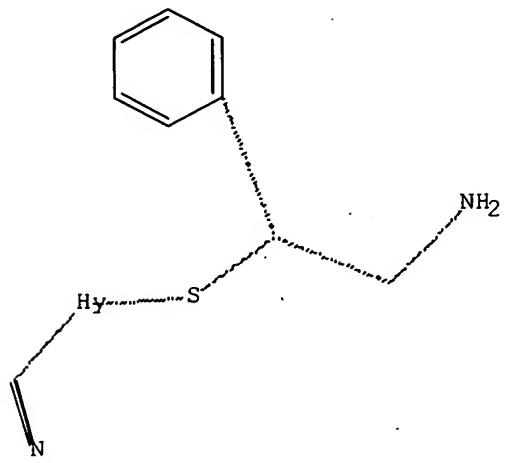


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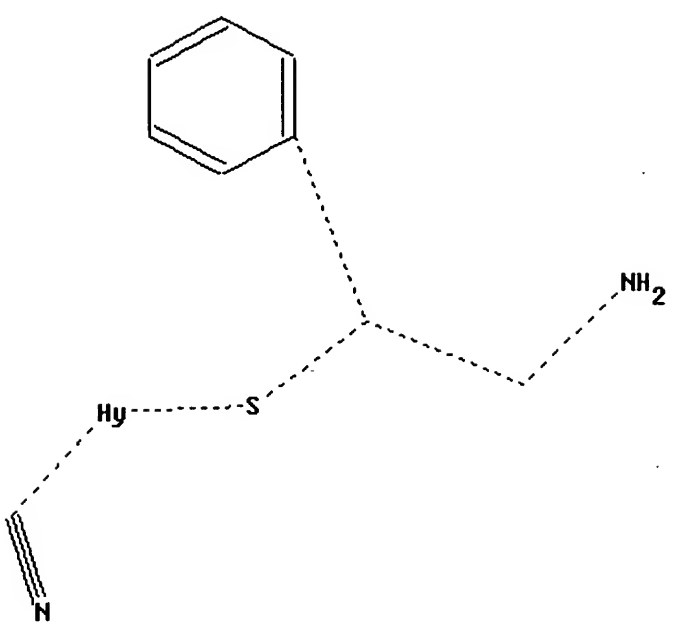

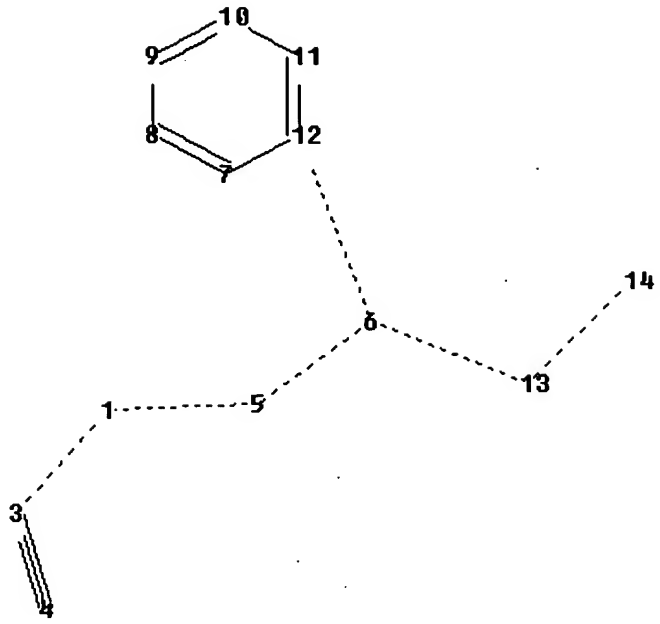

chain nodes :
1 3 4 5 6 13 14
ring nodes :
7 8 9 10 11 12
chain bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-3 1-5 3-4 5-6 6-12 6-13 13-14
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

Match level :
1:Atom 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom
12:Atom 13:CLASS 14:CLASS
Generic attributes :
1:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Number of Hetero Atoms : Exactly 1
Type of Ring System : Monocyclic

Element Count :
Node 1: Limited
C,C4
S,S1

L47 14 SEA FILE=MARPAT SSS FUL L42
L48 4 SEA FILE=MARPAT ABB=ON PLU=ON L47/COM

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=> s L48 not L53
             4 L53
L57          3 L48 NOT L53

=> dup rem L56 L57
FILE 'CAPLUS' ENTERED AT 09:46:10 ON 20 FEB 2007
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PROCESSING COMPLETED FOR L56
PROCESSING COMPLETED FOR L57
L58          17 DUP REM L56 L57 (0 DUPLICATES REMOVED)
                ANSWERS '1-14' FROM FILE CAPLUS
                ANSWERS '15-17' FROM FILE MARPAT

=> d ibib abs hitstr L58 1-14; d ibib abs qhit L58 15-17

L58  ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2004:182584  CAPLUS  Full-text
DOCUMENT NUMBER:          140:235710
TITLE:                    Preparation of 2-(4-substituted-2-oxo-1,2-
                          dihydropyridin-3-yl)-benzimidazoles as novel tyrosine
                          kinase inhibitors
INVENTOR(S):              Wittman, Mark D.; Balasubramanian, Neelakantan;
                          Velaparthi, Upender; Zimmermann, Kurt; Saulnier, Mark
                          G.; Liu, Peiying; Sang, Xiaopeng; Frennesson, David
                          B.; Stoffan, Karen M.; Tarrant, James G.; Marinier,
                          Anne; Roy, Stephan
PATENT ASSIGNEE(S):       Bristol-Myers Squibb Co., USA
SOURCE:                   U.S. Pat. Appl. Publ., 210 pp., Cont.-in-part of U.S.
                          Ser. No. 105,599.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     --------------       ----   --------    -------------------      --------
     US 2004044203         A1    20040304    US 2002-263448           20021002
     US 7081454            B2    20060725
     WO 2004031401         A2    20040415    WO 2003-US30931          20031001
     WO 2004031401         A3    20040729
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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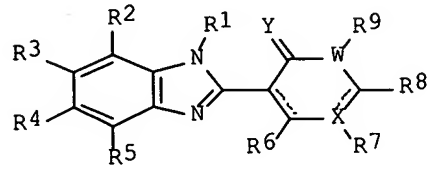
AU 2003282891	A1	20040423	AU 2003-282891	20031001
EP 1545543	A2	20050629	EP 2003-774510	20031001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006079518	A1	20060413	US 2005-289834	20051130
PRIORITY APPLN. INFO.:			US 2001-279327P	P 20010328
			US 2002-105599	A2 20020325
			US 2002-263448	A 20021002
			WO 2003-US30931	W 20031001

OTHER SOURCE(S): MARPAT 140:235710

GI



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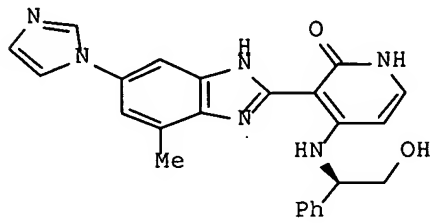


II

AB The title compds. [I; X = N, C, a bond, etc.; Y = O, S; W = N, C, O, S (if W = O or S, then R9 is absent); R1-R9 = H, alkyl, cycloalkyl, etc.] and their pharmaceutically acceptable salts which inhibit tyrosine kinase enzymes thereby making them useful as anti-cancer agents, were prepared Thus, reacting 3-[6-(imidazol-1-yl)-4-methyl-1H-benzimidazol-2-yl]-4-iodo- 1H-pyridin-2-one (preparation given) with (S)-(-)-2-phenylglycinol in the presence of N-methylmorpholine in DMF afforded 52% (S)-II. The compds. I showed kinase activity of <25μM against one or more of the following kinases CDK, EMT, FAK, Her1, Her2, IGF, IR, LCK, MET, PDGF, VEGF. The compds. I are also useful for the treatment of other diseases which can be treated by inhibiting tyrosine kinase enzymes.

IT ***468737-44-2P***

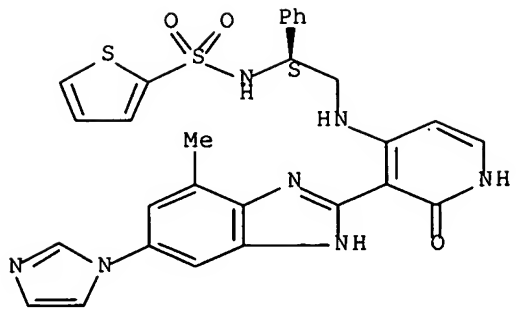
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(4-substituted-2-oxo-1,2-dihydropyridin-3-yl)-benzimidazoles as novel tyrosine kinase inhibitors)

RN 468737-44-2 CAPLUS

CN 2-Thiophenesulfonamide, N-[(1S)-2-[[1,2-dihydro-3-[6-(1H-imidazol-1-yl)-4-methyl-1H-benzimidazol-2-yl]-2-oxo-4-pyridinyl]amino]-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:777929 CAPLUS Full-text
DOCUMENT NUMBER: 137:294954
TITLE: Preparation of 2-(4-substituted-2-oxo-1,2-dihydropyridin-3-yl)-benzimidazoles as novel tyrosine kinase inhibitors
INVENTOR(S): Wittman, Mark D.; Balasubramanian, Neelakantan; Velaparthi, Upender; Zimmermann, Kurt; Saulnier, Mark G.; Liu, Peiying; Sang, Xiaopeng; Frennesson, David B.; Stoffan, Karen M.; Tarrant, James G.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 249 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079192	A1	20021010	WO 2002-US9402	20020326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442428	A1	20021010	CA 2002-2442428	20020326
EP 1381598	A1	20040121	EP 2002-723631	20020326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300475	A	20040216	EE 2003-475	20020326
CN 1514833	A	20040721	CN 2002-810516	20020326
JP 2004534010	T	20041111	JP 2002-577817	20020326
BR 2002008373	A	20050222	BR 2002-8373	20020326
HU 200400323	A2	20051128	HU 2004-323	20020326
ZA 2003007466	A	20050113	ZA 2003-7466	20030925
NO 2003004308	A	20031126	NO 2003-4308	20030926
BG 108206	A	20041130	BG 2003-108206	20030926

PRIORITY APPLN. INFO.: US 2001-279327P P 20010328
WO 2002-US9402 W 20020326

OTHER SOURCE(S): MARPAT 137:294954

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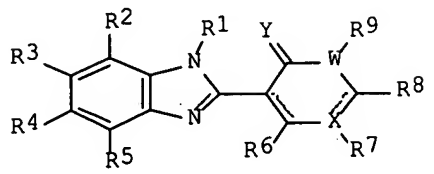

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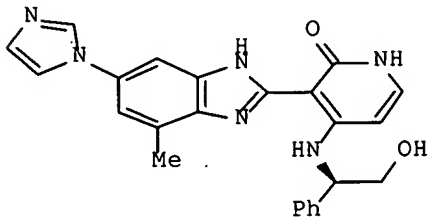


II

AB The title compds. [I; X = N, C, a bond, etc.; Y = O, S; W = N, C, O, S (if W = O or S, then R9 is absent); R1-R9 = H, alkyl, cycloalkyl, etc.] and their pharmaceutically acceptable salts which inhibit tyrosine kinase enzymes thereby making them useful as anti-cancer agents, were prepared Thus, reacting 3-[6-(imidazol-1-yl)-4-methyl-1H-benzimidazol-2-yl]-4-iodo- 1H-pyridin-2-one (preparation given) with (S)-(-)-2-phenylglycinol in the presence of N-methylmorpholine in DMF afforded 52% (S)-II which showed IC50 of 1.0 μM in cytotoxicity assay (HT-29 human colon tumor cell line). 30 Of the exemplified compds. I showed kinase activity of <25μM against one or more of the following kinases CDK, EMT, FAK, Her1, Her2, IGF, IR, LCK, MET, PDGF, VEGF. The compds. I are also useful for the treatment of other diseases which can be treated by inhibiting tyrosine kinase enzymes.

IT ***468737-44-2P***

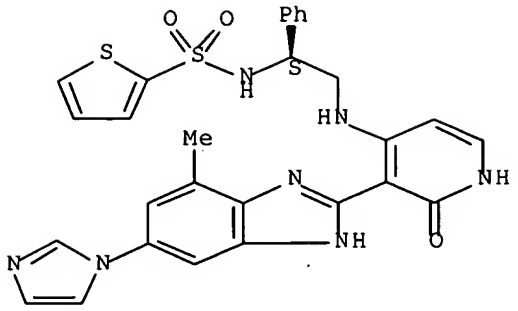
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 2-(4-substituted-2-oxo-1,2-dihydropyridin-3-yl)-benzimidazoles as novel tyrosine kinase inhibitors)

RN 468737-44-2 CAPLUS

CN 2-Thiophenesulfonamide, N-[(1S)-2-[[1,2-dihydro-3-[6-(1H-imidazol-1-yl)-4-methyl-1H-benzimidazol-2-yl]-2-oxo-4-pyridinyl]amino]-1-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:107321 CAPLUS Full-text
DOCUMENT NUMBER: 136:167373
TITLE: Preparation of imidazolyl derivatives as agonists or antagonists of somatostatin receptors
INVENTOR(S): Thurieau, Christophe Alain; Poitout, Lydie Francine; Galcera, Marie-Odile; Gordon, Thomas D.; Morgan, Barry A.; Moinet, Christophe Philippe; Bigg, Dennis
PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'applications Scientifiques (S.C.R.A.S.), Fr.
SOURCE: PCT Int. Appl., 369 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002010140	A2	20020207	WO 2001-US23959		20010731
WO 2002010140	A3	20020808			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2417204	A1	20020207	CA 2001-2417204		20010731
EP 1305294	A2	20030502	EP 2001-957342		20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004518613	T	20040624	JP 2002-516272		20010731
NZ 523774	A	20040924	NZ 2001-523774		20010731
NO 2003000473	A	20030130	NO 2003-473		20030130
US 2007032653	A1	20070208	US 2003-333556		20031020
PRIORITY APPLN. INFO.:			US 2000-222584P	P	20000801
			WO 2001-US23959	W	20010731

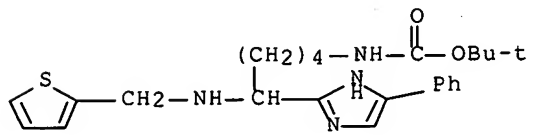
OTHER SOURCE(S): MARPAT 136:167373
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

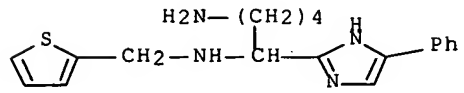
AB Imidazole derivs. I [R1 = H, (CH2)mCO(CH2)mZ1, (CH2)mZ1, etc.; Z1 = (un)substituted benzo[b]thiophene, Ph, naphthyl, etc.; m = 0-6; R2 = H, alkyl; R1 and R2 taken together with the nitrogen atoms to which they are attached form II-IV; R3 = (CH2)mE(CH2)mZ2; E = O, S, CO, etc.; Z2 = H, alkyl, NH2, etc.; R4 = H, (CH2)mA1; A1 = C(:Y)NX1X2; C(:Y)X2; C(:NH)X2, X2; Y = O, S; X1 = H, alkyl, etc.; X2 = alkyl, etc.; R5 = alkyl, (un)substituted aryl, etc.; R6 = H, alkyl; R7 = alkyl, (CH2)mZ4; Z4 = (un)substituted Ph, naphthyl, indolyl, etc.], which are useful as agonists or antagonists of somatostatin receptors (no data) and for inhibiting the proliferation of Helicobacter pylori, were prepared Thus, activating 2-furancarboxylic acid with carbonyldiimidazole followed by addition of 2-{(1S)-1-amino-2-(indol-3-yl)ethyl}-4-phenyl-1H-imidazole afforded 94% the title compound V. Compds. I are effective at 0.01-10.0 mg/kg/day.

IT *252301-98-7P 252306-26-6P*
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazolyl derivs. as agonists or antagonists of somatostatin receptors)

RN 252301-98-7 CAPLUS
CN Carbamic acid, [5-(4-phenyl-1H-imidazol-2-yl)-5-[(2-thienylmethyl)amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 252306-26-6 CAPLUS
CN 1,5-Pentanediamine, 1-(4-phenyl-1H-imidazol-2-yl)-N1-(2-thienylmethyl)- (9CI) (CA INDEX NAME)



L58 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:279860 CAPLUS Full-text
DOCUMENT NUMBER: 135:62958
TITLE: The Chemical Development of CI-972 and CI-1000: A Continuous Nitration, A MgCl2/Et3N-Mediated C-Alkylation of a Chloronitropyrimidine, A Catalytic

Protodediazotization of a Diazonium Salt, and an Air Oxidation of an Amine

AUTHOR(S): De Jong, Randall L.; Davidson, James G.; Dozeman, Gary J.; Fiore, Philip J.; Giri, Punam; Kelly, Margaret E.; Puls, Timothy P.; Seamans, Ronald E.

CORPORATE SOURCE: Pfizer Global Research and Development Holland Laboratories, Holland, MI, 49424, USA

SOURCE: Organic Process Research & Development (2001), 5(3), 216-225
CODEN: OPRDFK; ISSN: 1083-6160

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Efficient, large-scale processes were developed for the preparation of the potent PNP inhibitors: 2,6-diamino-3,5-dihydro-7-(3-thienylmethyl)-4H-pyrrolo[3,2-d]pyrimidin-4-one hydrochloride monohydrate and 2-amino-3,5-dihydro-7-(3-thienylmeth- yl)-4H-pyrrolo[3,2-d]pyrimidin-4-one hydrochloride monohydrate (I). We report (1) a safe, continuous nitration process for the preparation of 2-amino-6-chloro-5-nitro-4-pyrimidinol and its stable diisopropylamine salt, (2) the first MgCl2/Et3N-mediated C-alkylation of a chloronitropyrimidine, (3) a rare catalytic protodediazotization of 2-amino-4-oxo-7-thiophen-3-ylmethyl-4,5-dihydro-3H- pyrrolo[3,2-d]pyrimidine-6-diazonium chloride, (4) a single-step process to prepare I directly from 2-amino-6-hydroxy-5-nitro-α-(3- thienylmethyl)-4-pyrimidineacetonitrile using a sponge nickel-catalyzed reduction, and (5) a method to convert the over-reduction byproduct: 2,5-diamino-6-(1-aminomethyl-2-thiophen-3-yl-ethyl)-pyrimidin-4-ol into I using air oxidation

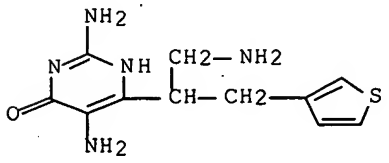
IT ***345906-77-6P***

RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)

(chemical development of CI-972 and CI-1000 (PNP inhibitors): continuous nitration and subsequent MgCl2/Et3N-mediated C-alkylation of chloronitropyrimidine, catalytic protodediazotization of diazonium salt, and air oxidation of amine)

RN 345906-77-6 CAPLUS

CN 4(1H)-Pyrimidinone, 2,5-diamino-6-[1-(aminomethyl)-2-(3-thienyl)ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 17 CAPLUS

ACCESSION NUMBER: 1999:795794 CAPLUS Full-text

DOCUMENT NUMBER: 132:35701

TITLE: Preparation of imidazolyl derivatives as as agonists or antagonists of somatostatin receptors

INVENTOR(S): Thurieau, Christophe Alain; Poitout, Lydie Francine; Galcera, Marie-Odile; Gordon, Thomas D.; Morgan, Barry; Moinet, Christophe Philippe

PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques, S.A., Fr.
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964401	A2	19991216	WO 1999-US12760	19990608
WO 9964401	A3	20030417		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2334945	A1	19991216	CA 1999-2334945	19990608
AU 9944257	A	19991230	AU 1999-44257	19990608
AU 746963	B2	20020509		
EP 1086086	A1	20010328	EP 1999-927323	19990608
EP 1086086	B1	20041013		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
HU 200202648	A2	20021228	HU 2002-2648	19990608
JP 2003523921	T	20030812	JP 2000-553410	19990608
AT 279396	T	20041015	AT 1999-927323	19990608
PT 1086086	T	20050228	PT 1999-927323	19990608
ES 2229718	T3	20050416	ES 1999-927323	19990608
RU 2263111	C2	20051027	RU 2001-101429	19990608
IL 139835	A	20051120	IL 1999-139835	19990608
TW 245758	B	20051221	TW 1999-88109822	19990811
NO 2000006267	A	20010207	NO 2000-6267	20001211
HK 1031873	A1	20050304	HK 2001-102404	20010403
US 6852725	B1	20050208	US 2001-719457	20010613
US 2004176379	A1	20040909	US 2004-771725	20040204
NO 2006000154	A	19991213	NO 2006-154	20060110
PRIORITY APPLN. INFO.:			US 1998-89087P P	19980612
			US 1998-96431 A1	19980612
			WO 1999-US12760 W	19990608
			US 2001-719457 A3	20010613

OTHER SOURCE(S): MARPAT 132:35701
GI

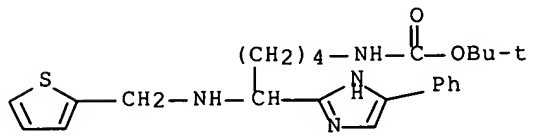
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1 = H, (CH2)mCO(CH2)mZ1, (CH2)mZ1, etc.; Z1 = (un)substituted benzo[b]thiophene, Ph, naphthyl, etc.; R2 = H, alkyl; R1 and R2 taken together with the nitrogen atoms to which they are attached form II-IV; R3 = (CH2)mE(CH2)mZ2; E = O, S, CO, etc.; Z2 = H, alkyl, NH2, etc.; R4 = H, (CH2)mA1; A1 = C(:Y)NX1X2; C(:Y)X2; C(:NH)X2, X2; Y = O, S; X1 = H, alkyl, etc.; X2 = alkyl, etc.; R5 = alkyl, (un)substituted aryl, etc.; R6 = H, alkyl; R7 = alkyl, (CH2)mZ4; Z4 = (un)substituted Ph, naphthyl, indolyl, etc.; m = 0-

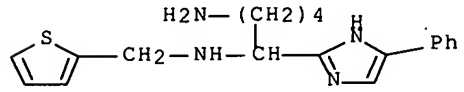
6] which are useful as agonists or antagonists of somatostatin receptors (no data), and for inhibiting the proliferation of Helicobacter pylori, were prepared Thus, activating 2-furancarboxylic acid with carbonyldiimidazole followed by addition of 2-{(1S)-1-amino-2-(indol-3-yl)ethyl}-4-phenyl-1H-imidazole afforded 94% the title compound V. Compds. I are effective at 0.01-10.0 mg/kg/day.

IT *252301-98-7P 252306-26-6P*
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazolyl derivs. as as agonists or antagonists of somatostatin receptors)

RN 252301-98-7 CAPLUS
CN Carbamic acid, [5-(4-phenyl-1H-imidazol-2-yl)-5-[(2-thienylmethyl)amino]pentyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 252306-26-6 CAPLUS
CN 1,5-Pentanediamine, 1-(4-phenyl-1H-imidazol-2-yl)-N1-(2-thienylmethyl)-(9CI) (CA INDEX NAME)



L58 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:516053 CAPLUS Full-text
DOCUMENT NUMBER: 127:233996
TITLE: Regioselective photoaddition of amine to styrylthiophenes
AUTHOR(S): Ho, T. I.; Ho, C. S.; Shin, S. M.; Pa, K.
CORPORATE SOURCE: Department Chemistry, National Taiwan University, Taipei, Taiwan
SOURCE: Electronic Conference on Heterocyclic Chemistry, [Proceedings], June 24-July 22, 1996 (1997), Meeting Date 1996, No pp. given. Editor(s): Rzepa, Henry S.; Snyder, James P.; Leach, Christopher. Royal Society of Chemistry: Cambridge, UK.
CODEN: 64WTAX
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English

AB A symposium. The photochem. of styrylthiophene(ST) and its derivs. with amines is investigated. Exciplex emission for tertiary amines and 3-ST systems have been observed Photochem. addition of tertiary and secondary

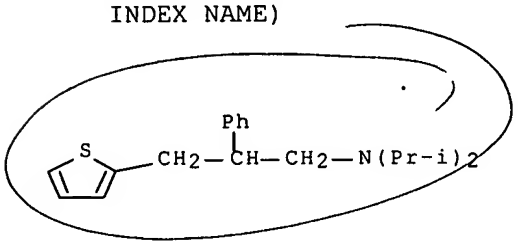
amines to 2-ST are non-regioselective. Photoaddn. of ammonia to 2-ST sensitized by dicyano benzene is regioselective. The difference in the photochem. behavior is compared.

IT *195059-18-8P*

RL: SPN (Synthetic preparation); PREP (Preparation)
(mechanistic reaction intermediate; regioselective photoaddn. of amine to styrylthiophenes)

RN 195059-18-8 CAPLUS

CN 2-Thiophenepropanamine, N,N-bis(1-methylethyl)-β-phenyl- (9CI) (CA INDEX NAME)



L58 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:531729 CAPLUS Full-text

DOCUMENT NUMBER: 113:131729

TITLE: Preparation and formulation of 3-(arylthio)benzenepropanamines and analogs as inhibitors for serotonin and norepinephrine uptake.

INVENTOR(S): Foster, Bennie J.; Hunden, David C.; Lavagnino, Edward R.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 12 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4902710	A	19900220	US 1988-284501	19881214
EP 373836	A1	19900620	EP 1989-312829	19891208
EP 373836	B1	19940316		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
AT 102920	T	19940415	AT 1989-312829	19891208
CA 2005173	A1	19900614	CA 1989-2005173	19891211
JP 02218661	A	19900831	JP 1989-324878	19891212
PRIORITY APPLN. INFO.:			US 1988-284501 A	19881214
			EP 1989-312829 A	19891208

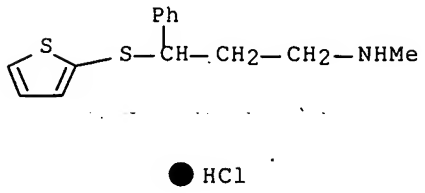
OTHER SOURCE(S): MARPAT 113:131729

AB RSOnCHR1CH2CH2NR3R4 [I; R = (un)substituted Ph, naphthyl, thienyl, furanyl, pyrrolyl; R1 = cycloalkyl, furanyl, pyridyl, thiazolyl, (un)substituted Ph, thienyl; R2, R3 = H, Me; n = 0-2], inhibitors for the uptake of serotonin and norepinephrine and therefore useful as antidepressants, antianxiety agents, and antiobesity agents, were prepared Thus, PhCH2NHMe was refluxed with HCHO and PhCOMe in ethanolic HCl and the product reduced with NaBH4 to give, after deprotection, HOCHPhCH2CH2NHMe which was treated with SOCl2 and the product condensed with 2-MeOC6H4SH to give 2-MeOC6H4SCHPhCH2CH2NHMe which had IC50 of 270 and 42 nM for inhibition of synaptosomal uptake of serotonin and norepinephrine, resp., in vitro.

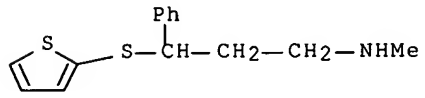
IT *128036-43-1P 128036-44-2P 128036-45-3P*

128036-46-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as serotonin and norepinephrine uptake inhibitor)

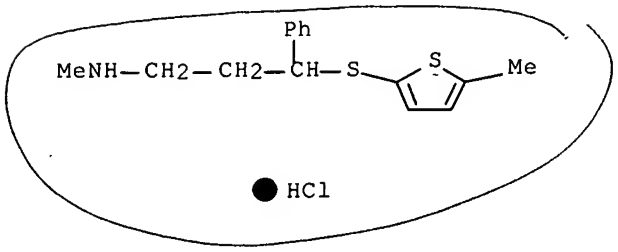
RN 128036-43-1 CAPLUS
CN Benzenepropanamine, N-methyl-γ-(2-thienylthio)-, hydrochloride (9CI) (CA INDEX NAME)



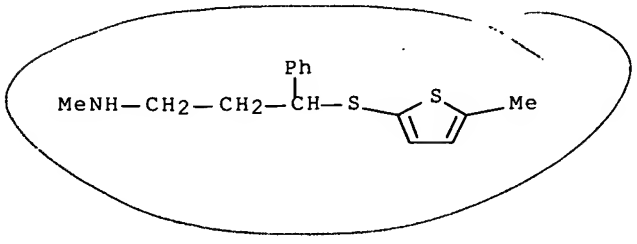
RN 128036-44-2 CAPLUS
CN Benzenepropanamine, N-methyl-γ-(2-thienylthio)- (9CI) (CA INDEX NAME)



RN 128036-45-3 CAPLUS
CN Benzenepropanamine, N-methyl-γ-[(5-methyl-2-thienyl)thio]-, hydrochloride (9CI) (CA INDEX NAME)



RN 128036-46-4 CAPLUS
CN Benzenepropanamine, N-methyl-γ-[(5-methyl-2-thienyl)thio]- (9CI) (CA INDEX NAME)

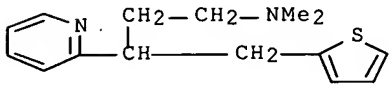


L58 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:29310 CAPLUS Full-text
DOCUMENT NUMBER: 49:29310
ORIGINAL REFERENCE NO.: 49:5666h-i,5667a
TITLE: Prophenpyridamine (Trimeton) and chlorprophenpyridamine (Chlortrimeton)
AUTHOR(S): Labelle, Annette; Tislow, Richard
CORPORATE SOURCE: Schering Corp., Bloomfield, NJ
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1955), 113, 72-88
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

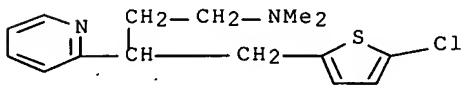
AB A series of 70 compds., including γ,γ-disubstituted N,N-dialkylpropylamines (Sperber, et al., C.A. 47, 575i), pyridyl-substituted alkamine ethers (S., et al., C.A. 45, 4265h), pyridyl aryloxy alkamine ethers (Papa, et al., C.A. 45, 9542c), and amides of ethylenediamine (Villani, et al., C.A. 44, 10176a), were tested for antihistaminic, antispasmodic, toxic, and other pharmacol. properties. As antihistaminics, Chlortrimeton and Clistin (paracarbinoxamine) were many times as potent as Trimeton, a few others were about as potent as Trimeton, and the remainder had low activity or were inactive. The toxicity of Trimeton and Chlortrimeton is low.

IT ***672304-71-1***, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]-
717922-20-8, Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]-
(pharmacol. of)

RN 672304-71-1 CAPLUS
CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



RN 717922-20-8 CAPLUS
CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:32576 CAPLUS
DOCUMENT NUMBER: 49:32576
ORIGINAL REFERENCE NO.: 49:6316f-i,6317a-i,6318a-c
TITLE: 3-Pyridylpropylamine antihistaminic substances
INVENTOR(S): Sperber, Nathan; Papa, Domenick; Schwenk, Erwin
PATENT ASSIGNEE(S): Schering Corp.
DOCUMENT TYPE: Patent

LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2676964		19540427	US 1950-166768	19500607

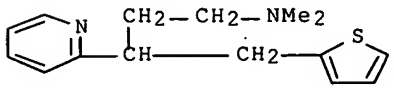
AB Heterocyclic substituted aliphatic amines having antihistaminic and antianaphytactic activity are described, XCHR(CH2)nR', where X is a heterocyclic group which may be substituted, n is not less than 2 nor more than 4, R is alkyl, aralkyl, aryl, cycloalkyl, or heterocyclic group or a Cl or Br derivative of such groups, and R' is dialkylamino, piperidino, morpholino, or imidazolino group. To 1.0 mol KNH2 in 3 l. liquid NH3 is added 1.0 mol 2-benzylpyridine (I), then after 15 min. 1 mol Me2NCH2CH2Cl (II) added, the NH3 allowed to evaporate, the product decomposed with H2O, extracted with Et2O, the Et2O layer dried, evaporated, and distilled to give 3-phenyl-3-(2-pyridyl)-N,N-dimethylpropylamine, b1-2 139-42°. The 3-(2,3-dimethoxyphenyl) analog was obtained as follows. A mixture of 2,3-(MeO)2C6H3CHO 10, picolinic acid 4, and cymene 25 was heated 4-6 h. at 160-70°, cooled, the product extracted with aqueous HCl, the acid exts. made alkaline with gaseous NH3, the mixture extracted with Et2O, washed, dried, evaporated, and distilled to give (2-pyridyl)-2,3-dimethoxy-phenylcarbinol (III). To a solution of III 10 in anhydrous C6H6 60 cooled to 0°, there was added dropwise SOCl2 6.5, the reaction allowed to reach room temperature, let stand several hrs., the excess SOCl2 cautiously decomposed with 10% K2CO3 until the mixture was strongly alkaline, the C6H6 layer separated, dried, filtered, and vacuum concentrated, the deep red residue reduced with Zn and AcOH, stirred 6 h., and worked up to give 2-(2,3-dimethoxybenzyl)pyridine (IV). Condensation of IV with II as above yielded 3-(2,3-dimethoxyphenyl)-3-(2- pyridyl)-N,N-dimethylpropylamine, b1-2 195-200°. Similarly prepared were the following substituted Ph analogs: 3,4-(OMe)2, 2,4-Cl2, 2,4-Me2, 4-Me2N, 4-NH2 acetylated to 4-AcNH. Condensation of I with β-piperidinoethyl chloride with KNH2 in liquid NH3 gave 3-phenyl-3-(2-pyridyl)-1-piperidinopropane. The morpholino analog was obtained in the same way with β-morpholinoethyl chloride. Condensation of α-picoline and 2-thienylmethyl chloride with KNH2 in liquid NH3 gave 1-(2-pyridyl)-2-(2-thienyl)ethane (V), b0.5 106-10°. V and Br in AcOH at 10° gave 1-(5-bromo-2-thienyl)-2-(2- pyridyl)ethane (VI), b0.5 129-33°. VI and II in the usual way gave 4-(5-bromo-2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, light yellow oil, b0.5 145-8°. The corresponding 5-Cl analog b0.5 140-4°, was prepared similarly. Treating 1 mol 2-hexylpyridine in Et2O with BuLi in Et2O in a N atmospheric, after refluxing several hrs. II added, the mixture refluxed 6 h., the product decomposed with H2O, the Et2O layer separated, dried, and distilled gave 3-(2-pyridyl)-N,N-dimethyloctylamine, b1.5 104-5°. In the same way from 2-pyridyl-N,N-dimethylpropylamine and bromocyclohexane, there was obtained 3-cyclohexyl-3-(2-pyridyl)-N,N- dimethylpropylamine, b2 145-50°; similarly, 1-(2-pyridyl)-1-phenyl- 2-(2-imidazolinyl)ethane from I and 2-chloromethyl)imidazoline; 2-(2-pyridyl)-1-phenyl-3-(2-imidazolinyl)propane, b1 143-6°, from stilbazole and 2-(chloromethyl)imidazoline; 3-(2-thienyl)-3-(2-pyridyl)- N,N-dimethylpropylamine, b1 125-8°, from 2-(thienyl)pyridine, b1 103-6° (from 2-thienyl-1-(2-pyridyl)carbinol, b1 138-40°, followed by treatment with SOCl2, and Zn-AcOH reduction) and II; 3-(3-thienyl)-3-(2-pyridyl)-N,N-dimethylpropylamine, b2-3 134-7°, from (3-thienyl)(2-pyridyl)carbinol, b1 141-3°, converted to 2-(3-thenyl)pyridine, b0.5 105-7°, and II; 3-(5-methyl-2-thienyl)-3- (2-pyridyl)-N,N-dimethylpropylamine, b1 134-7°, from (5-methyl-2-thienyl)(2-pyridyl)carbinol, b1 146-50°, converted to 2-(5-methyl-2-thenyl)pyridine, b0.5 108-11°, and II; 3-(2-thienyl)-3-(2-pyridyl)-N,N-diethylpropylamine, yellow oil, b1 130-2°; 3-(3-methyl-2-thienyl)-3-(2-pyridyl)-N,N- diethylpropylamine, b2-3 138-42°; 3-(5-chloro-2-thienyl)-3-(2-

pyridyl)-N,N-dimethylpropylamine, b1-2 142-5°; 3-(3-methyl-5-chloro- 2-thienyl)-3-(2-pyridyl)-N,N-dimethylpropylamine, pale yellow oil, b1 149-52°; 3-(2-thienyl)-3-(6-methyl-2-pyridyl)-N,N- dimethylpropylamine; yellow-orange oil, b1-2 133-7°; 3-(5-methyl-2-thienyl)-3-(2-pyridyl)-1-piperidinopropane, yellow oil, b0.5-1 140-4°; 3-(5-bromo-2-thienyl)-3- (2-pyridyl)- N, N-dimethylpropylamine, b1-2 150-5° from (5-bromo-2-thienyl)(2- pyridyl) carbinol, b1 152-5°. To 400 g. α-phenyl-α- (β-dimethylaminoethyl-2-pyridylacetonitrile, there is added 2 kg. 80% H_2SO_4, the mixture heated 24 h. with stirring at 140-50°, decomposed with ice and H_2O, made alkaline with NH_3 gas, the oil extracted with Et_2O, dried, evaporated, and distilled to give 3-phenyl-3-(2-pyridyl)-N,N-dimethylpropylamine, b1-2 139-42°. The following compds. were prepared similarly from the corresponding nitriles: 3-phenyl-3-(2-pyridyl)-N,N-diethylpropylamine, b1 156°; 4-phenyl-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.5 135°; 3-(2-thienyl)-3-(2-pyridyl)-N,N-dimethylpropylamine, pale yellow oil, b1 125-8°; 4-(2-thienyl)-3-(2-pyridyl)-N,N- dimethylbutylamine, b0.1 130-3°; 3-(p-tolyl)-3-(2-pyridyl)-N,N-dimethylpropylamine, b0.5 130-5°; 3-(p-methoxyphenyl)-3-(2-pyridyl)- N,N-dimethylpropylamine, b0.5 137-42°; 3-(p-isopropylphenyl)-3-(2- pyridyl)-N,N-dimethylpropylamine, b1 144-7°; 3-phenyl-3-(6-methyl-2- pyridyl)-N,N-dimethylpropylamine, b1 171-5°; 3-(p-bromophenyl)-3-(2- pyridyl)- N,N-dimethylpropylamine, b0.5 147-52°; 4-phenyl-4-(2-pyridyl)-2-(dimethylamino)butane; 4-phenyl-4-(2-pyridyl)-N,N- dimethylbutylamine; 3-cyclohexyl-3-(2-pyridyl)-N,N-dimethylpropylamine; 4-cyclohexyl-3-(2-pyridyl)-N,N-dimethylbutylamine; 3-(5-bromo-2-thienyl)-3- (2-pyridyl)- N,N-dimethylpropylamine ; 4-(p-bromophenyl)-3-(2-pyridyl)-N,N- dimethylbutylamine; 3-(p-chlorophenyl)-3-(2-pyridyl)-N,N- dimethylpropylamine; 3-(o-chlorophenyl)-3-(2-pyridyl)-N,N- dimethylpropylamine. Condensation of 227 g. 2-chloropyridine, 41 g. MeCN, 1 l. PhMe, and $NaNH_2$ (from 51 g. Na) gave 94 g. α,α-bis(2- pyridyl) acetonitrile, b1 182-92°, m. 137-9° (from C_6H_6-petr. ether); this (49 g.), 300 cc. PhMe, 32 g. $Me_2NCH_2CH_2Cl$, and $NaNH_2$ (from 7 g. Na) gave α,α-bis(2-pyridyl)-α-(2- dimethylaminoethyl)acetonitrile, deep red, viscous oil, b0.5 165-72°, which (25 g.) with 135 g. 70% H_2SO_4 were heated 5 h at 130° with stirring until CO_2 evolution ceased, poured on ice, made alkaline with NH_4OH, extracted with Et_2O, dried, filtered, evaporated, and distilled to give 3,3-bis(2-pyridyl)-N,N-dimethylpropylamine, b0.5 129-32°. A mixture of 2-furanacetonitrile (0.5 mol), 2-chloropyridine (0.5 mol), 2-dimethylaminoethyl chloride (0.5 mol) in 500 cc. PhMe, and $NaNH_2$ (1 mol) similarly gave 3-(2-furyl)-3-(2-pyridyl)-N,N-dimethylpropylamine. Similarly, 3-(2-pyridyl)-3-(2-thiazolyl)-N,N-dimethylpropylamine, pale yellow oil, b2 138-40°; 3-(2-pyridyl)-3-(2-thiazolyl)-N,N- diethylpropylamine; 3-(2-pyridyl)-3-(2-pyrimidyl)-N,N-dimethylpropylamine, colorless oil, b1 135-40°; 3,3-bis(2-thiazolyl)-N,N- dimethylpropylamine; 4,4-bis(2-thiazolyl)-N,N-dimethylbutylamine; 3-(2-pyrimidyl)-3-(2-thiazolyl)-N,N-dimethylpropylamine; 2-dimethylamino-4-(2-pyrimidyl)-4-(2-thiazolyl)-butane; 3-(2-thiazolyl)-3-(2-thienyl)-N,N-dimethylpropylamine; 3-(2-thiazolyl)-3-(2-thienyl)-1-piperidinopropane; 3-(2-pyrazinyl)-3-(2- thiazolyl)-N,N-dimethylaminopropane; 3-(2-pyrazinyl)-3-(2-thiazolyl)-N,N- dimethylaminopropane; 3-(2-thiazolyl)-3-(2-furyl)-N,N-dimethylpropylamine; 3-(2-thienyl) -3-(2-pyridyl)-N,N-dimethylpropylamine, pale yellow oil, b2 154°. To 1 mol of KNH_2 in 3 l. liquid NH_3 is added 1 mol α-picoline, and 15 min. later 1.1 mol 2-thienylmethyl chloride, the NH_3 evaporated, the product decomposed with H_2O, extracted with Et_2O, the Et_2O layer extracted with dilute HCl, the acid layer made ammoniacal, the oil extracted with Et_2O, dried, concentrated, and distilled to give 1-(2-thienyl)-2-(2-pyridyl)ethane, b0.5 106-10°; bromination in HOAc gave 1-(5-bromo-2-thienyl)-2-(2- pyridyl)ethane, b0.5 129-33°, which condensed with Me_2-NCH_2CH_2Cl gave 4-(5-bromo-2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, light yellow oil, b0.5 145-8°, and in the same manner, the 5-chloro analog, b0.5 140-4°, and 4-(2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.1 130-3°.

IT *672304-71-1P*, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]-
717922-20-8P, 2-Thiophenebutylamine, 5-chloro-N,N-dimethyl-γ-2-pyridyl- *873407-08-0P*, 2-Thiophenebutylamine, 5-bromo-N,N-dimethyl-γ-2-pyridyl-
RL: PREP (Preparation)
(preparation of)

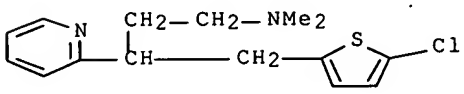
RN 672304-71-1 CAPLUS

CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



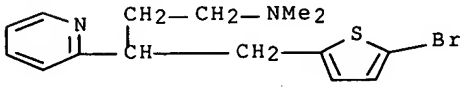
RN 717922-20-8 CAPLUS

CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



RN 873407-08-0 CAPLUS

CN Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1955:5015 CAPLUS

DOCUMENT NUMBER: 49:5015

ORIGINAL REFERENCE NO.: 49:1107g-i,1108a-g

TITLE: Heterocylic-substituted aliphatic amines

INVENTOR(S): Sperber, Nathan; Papa, Domenick; Schwenk, Erwin

PATENT ASSIGNEE(S): Schering Corp.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2656358		19531020	US 1950-178166	19500807

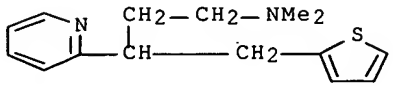
AB Previous (2-pyridylamino)alkanes are again described and new derivs. included. Condensation of 2-picoline and 2-thenyl chloride with KNH2 yields 1-(2-pyridyl)-2-(2-thienyl)ethane, b0.5 106-10°; Br treatment in HOAc results in 1-(5-bromo-2-thienyl)-2-(2-pyridyl)ethane, b0{cut=4,1}middot;5 129-33°, and condensation with Me2NCH2CH2Cl (I) gives 4-(5-bromo-2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.5 145-8°. The Cl analog, b0.5 140-4°, is similarly obtained. I condensed with 2-hexylpyridine in ethereal BuLi gives 3-(2-pyridyl)-N,N-dimethyloctylamine, b. 104-5°. 8-(2-Pyridyl)-N,N-dimethylpropylamine and C6H11Br similarly yield 3-cyclohexyl-3-(2-pyridyl)-N,N-dimethylpropylamine, b2 145-50°. KNH2 or BuLi condensation of 2-benzylpyridine with 2-(chloromethyl) imidazoline results in 1-(2-pyridyl)-1-phenyl-2-(2-imidazolinyl)ethane, and 2-phenethylpyridine gives the 2-substituted propane, b1 143-6°. BuLi condensation of 2-bromopyridine and 2-thiophenecarboxaldehyde at -30° gives (2-thienyl)(2-pyridyl)carbinol, b1.0 138-40°, which is treated 1 h. with SOCl2 in C6H6 below 25°, made alkaline with dilute NaOH below 30°, the organic layer concentrated in vacuo, the residue dissolved in HOAc, Zn dust added, and the acid mixture heated 6 h. at 90-5°, filtered, made alkaline, Et2O extracted, and distilled, giving 2-(2-thenyl)pyridine (II), b1.0 103-6°. I and II with KNH2 give 3-(2-thienyl)-3-(2-pyridyl)-N,N-dimethylpropylamine (III) b1.0 125-8°. Other 3-(2-pyridyl)propylamines obtained in the same sequence of reactions are 3-(3-thienyl), b2-3 134-7°, from (3-thienyl)(2-pyridyl)carbinol and 2-(3-thenyl)pyridine; 3-(5-methyl-2-thienyl), b1 134-7°, from 5-methyl-2- thiophenecarboxaldehyde; 3-(5-chloro-2-thienyl), b1.2 142-5°, from 5-chloro-2-thiophenecarboxaldehyde; 3-(3-methyl-5-chloro-2-thienyl), b1 149-52°, from the corresponding thiophene; 3-(2-thienyl)-3-(6- methyl-2-pyridyl), b1.2 133-7°, from 2-bromo-6-methylpyridine; and 3-(5-bromo-2-thienyl), b1-2 150-5°, from the bromothiophenecarboxaldehyde. The analogous diethylpropylamines, 3-(2-thienyl), b1 130-2°, and 3-(3-methyl-2-thienyl), b2.3 138-42°, are similarly obtained from the di-Et compound instead of I. 2-(5-Methyl-2-thenyl)pyridine, b0.6 108-11°, and 2-piperidinoethyl chloride give 3-(5-methyl-2-thienyl)-3-(2-pyridyl)-1-piperidinopropane, b. 140-4°. Compds. derived from nitriles but not previously listed are III, from (2-thienyl)(2-dimethylaminoethyl)(2-pyridyl)acetonitrile (IV); addnl. 3-(2-pyridyl)-N,N-dimethylpropylamines are 3-(p-tolyl), b0.5 130-5°, from the α-(p-tolyl) analog of IV; 3-phenyl-3-(6-methyl-2-pyridyl), b1 171-5°; 3-cyclohexyl, 4-cyclohexyl, 3-(5-bromo-2-thienyl), 3-(p-ClC6H4), and 3-(o-ClC6H4) from their corresponding nitriles. The benzylacetonitrile yields 4-phenyl-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.5 135°. A NaNH2 suspension (51 g. of Na) is added to 227 g. of 2-chloropyridine and 41 g. MeCN in 1 l. PhMe at 100°, the mixture refluxed 4 h., decomposed with H2O, extracted with dilute HCl, made alkaline with NH3, extracted with C6H6, distilled, and the residue, b1 182-92°, crystallized from petr. ether-C6H6, giving bis(2-pyridyl)acetonitrile, m. 137-9°, which with I and NaNH2 yields bis(2-pyridyl)(2-dimethylaminoethyl)acetonitrile, b0.5 165-72°, treatment of which with 70% H2SO4 5 h. at 130° gives 3,3-bis(2-pyridyl)-N,N-dimethylpropylamine, b0.5 129-32°. Similarly the 3-(2-furyl)-3-(2-pyridyl) analog is obtained from 2-furanacetonitrile; 3-(2-pyridyl-3-(2-thiazolyl), b2 138-40°, from 2-bromothiazole (V); 3-(2-pyridyl)-3-(2-pyrimidinyl), b1 135-40°, from 2-chloropyrimidine; 3,3-bis(2-thiazolyl), from the condensation of MeCN and V; 3-(2-pyrimidinyl)-3-(2-thiazolyl), from 2-chloropyrimidine condensed with MeCN, the resulting nitrile condensed with V, and the disubstituted nitrile treated with I, followed by the H2SO4 treatment. Me2NCHMeCH2Cl in place of I yields 2-dimethylamino-4-(2-pyrimidinyl)-4-(2- thiazolyl)butane. V and Et2NCH2CH2Cl give 3-(2-pyridyl)-3-(2-thiazolyl)- N,N-diethylpropylamine, and bis(2-thiazolyl)acetonitrile and Me2N(CH2)3Cl give 4,4-bis-(2-thiazolyl)-N,N-dimethylbutylamine. The reaction of 2-thenyl chloride with KCN in EtOH and treatment of the resulting nitrile as before gives 3-(2-thiazolyl)-3-(2-thienyl)-N,N-dimethylpropylamine. 2-Piperidinoethyl chloride gives the piperidinopropane. Addnl. dimethylpropylamines include 3-(2-pyrazinyl)-3-(2-thiazolyl), 3-(2-thiazolyl)-3-(2-furyl), and 3-(2-thienyl)-3-(2-pyridyl). In

essentially the same manner, the following 3-(2-pyridyl)-N,N-dimethylbutylamines are prepared; 4-(3-methyl-5-thiazolylmethyl); 4-(5-thiazolylmethyl), b0.5 138-40°; 4-(2-thienyl), b0.1 130-3°; 4-(2-furyl), b2-3 140-6°; 4-(2-pyrazinyl), b1-2 144-50°; and 3,4-di-(2-pyridyl)-N,N-dimethylbutylamine, b3.5 145-50°. These substances have antihistaminic properties when used either as the free bases or, as previously described, as salts of inorg. and organic acids. Cf. C.A. 46, 4574a.

IT ***672304-71-1P***, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]- ***717922-20-8P***, Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- ***873407-08-0P***, Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]-
RL: PREP (Preparation)
(preparation of)

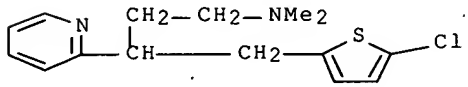
RN 672304-71-1 CAPLUS

CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



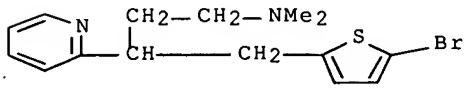
RN 717922-20-8 CAPLUS

CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



RN 873407-08-0 CAPLUS

CN Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1954:71925 CAPLUS

DOCUMENT NUMBER: 48:71925

ORIGINAL REFERENCE NO.: 48:12810i,12811a-f

TITLE: Aminoalkylheterocycles

INVENTOR(S): Sperber, Nathan; Papa, Domenick; Schwenk, Erwin

PATENT ASSIGNEE(S): Schering Corp.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2604473		19530722	US	

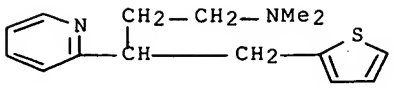
GI For diagram(s), see printed CA Issue.

AB Compds. of the formula RR'CHA (I) (A = tertiary aminoalkyl, R' = aryl or heterocycle, and R = heterocycle with a ring N adjacent to R'CHA), prepared by alkylation of RR'CH2 (II), are of value as antihistamines and antianaphthylactics. KNH2 1 and 2-PhCH2-C5H4N 1 mol in liquid NH3 3 l. gave with Me2NCH2CH2Cl (III) 1.1, Ph(2-Py)CHCH2CH2NMe2, (Py = pyridyl) (I, R = 2-Py, R' = Ph, A = Me2NCH2CH2), b1-2 139-42°, alternately prepared by alkaline or acid hydrolysis of RR'CACN (IV). From II were prepared the following I (R, R', A given, C2H4): 2-Py, 5-bromo-2-thenyl, Me2NC2H4 (V), b0.5 145-8° {from 2-[2-(2-pyridyl)ethyl]thiophene (Va), b0.5 106-10°, via the 5-Br derivative of Va, b0.5 129-33°}; 2-Py, 5-chloro-2-thenyl, Me2NC2H4, b0.5 140-4°; 2-Py, C5H11, Me2NC2H4, b1.5 104-5°; 2-Py, C6H11, Me2NC2H4, b2 145-50° (VI); 2-Py, Ph, CH2C:N.(CH2)2.NH; and 2-Py, PhCH2, CH2C:N.(CH2)2.NH, b1 143-6°. The following I were prepared from the corresponding IV: 2-Py, Ph, Et2NC2H4, b1 156°; 2-Py, PhCH2, Me2NC2H4, b0.5 135°; 2-Py, 2-thienyl, Me2NC2H4 (VII), b1 125-8°; 2-Py, 2-thenyl, Me2NC2H4, b0.1 130-3°; 2-Py, p-tolyl, Me2NC2H4, b0.5 130-5°; 2-Py, 4-MeOC6H4, Me2NC2H4, b0.5 137-42°; 2-Py, 4-Me2CHC6H4, Me2NC2H4, b1 144-7°; 6-methyl-2-pyridyl, Ph, Me2NC2H4, b1 171-5°; 2-Py, 4-BrC6H4, Me2NC2H4, b0.5 147-52°; 2-Py, Ph, Me2N(CH2)3; 2-Py, Ph, Me2NCHMeCH2; VI; 2-Py, 5-bromo-2-thienyl, Me2NC2H4, b1-2 150-5° (VIII); 2-Py, C6H11CH2, Me2NC2H4; 2-Py, 4-BrC6H4CH2, Me2NC2H4; 2-Py, 4-ClC6H4, Me2NC2H4; 2-Py, 2-ClC6H4, Me2NC2H4; 2-Py, 2-Py, Me2NC2H4, b0.5 129-32° [IV, b0.5 165-72°, from III and (2-Py)2CHCN, m. 137-9°, b1 182-92°]; 2-Py, 2-furyl, Me2NC2H4; 2-Py, 2-thiazolyl, Me2NC2H4 (from 2-chloropyridine and 2-bromothiazole either stepwise or simultaneously with MeCN, then III, or preferably the heterocycle with Me2NC2H4CN); 2-Py, 2-thiazolyl, Et2NC2H4; 2-Py, 2-pyrimidyl, Me2NC2H4, b1 135-40°; 2-thiazolyl, 2-thiazolyl, Me2NC2H4; 2-thiazolyl, 2-thiazolyl, Me2NC3H6; 2-thiazolyl, 2-pyrimidyl, Me2NC2H4; 2-thiazolyl, 2-pyrimidyl, Me2NCHMeCH2; 2-thiazolyl, 2-thienyl, Me2NC2H4; 2-thiazolyl, 2-thienyl, 2-piperidinoethyl; 2-thiazolyl, 2-pyrazinyl, Me2NC2H4; and 2-thiazolyl, 2-furyl, Me2NC2H4. 2,3-(MeO)2C6H3CHO 10 and picolinic acid 4 in refluxing cymene 25 g. for 4-6 h. gave RR'CHOH [where R = 2-Py, R' = 2,3-(MeO)2C6H3], converted to II by SOCl2, then Zn = HOAc and then to I, b1-2 195-200°, with III. Other I thus obtained (R and R' given): 2-Py, 3,4-(MeO)2C6H3, Me2NC2H4; 2-Py, 2,4-Cl2C6H3, Me2NC6H4; 2-Py, 2,4-Me2C6H2, Me2NC2H4; 2-Py, Ph, 2-piperidinoethyl; 2-Py, Ph, 2-morpholinoethyl; 2-Py, 4-Me2NC6H4, Me2NC2H4, b1.5 183-5°; 2-Py, 4-AcNHC6H4, Me2NC2H4; 2-Py, 4-H2NC6H4, Me2NC2H4; VIII; VII; 2-Py, 3-thienyl, Me2NC2H4, b2-3 134-7°; 2-Py, 5-methyl-2-thienyl, Me2NC2H4, b1 134-7°; 2-Py, 2-thienyl, Et2NC2H4, b1 130-2°; 2-Py, 3-methyl-2-thienyl, Et2NC2H4, b2-3 138-42°; 2-Py, 5-chloro-2-thienyl, Me2NC2H4, b1-2 142-5°; 2-Py, 5-chloro-3-methyl-2-thienyl, Me2NC2H4, b1 149-52°; 6-methyl-2-pyridyl, 2-thienyl, Me2NC2H4, b1-2 133-7°; and 2-Py, 5-methyl-2-thienyl, 2-piperidinoethyl, b0.5-1 140-4°.

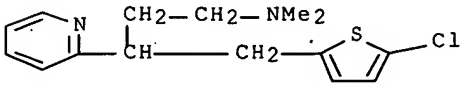
IT ***672304-71-1P***, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]-
717922-20-8P, 2-Thiophenebutylamine, 5-chloro-N,N-dimethyl-γ-2-pyridyl- ***873407-08-0P***, Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]-
RL: PREP (Preparation)
(preparation of)

RN 672304-71-1 CAPLUS

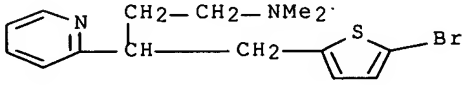
CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



RN 717922-20-8 CAPLUS
CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



RN 873407-08-0 CAPLUS
CN Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:24179 CAPLUS
DOCUMENT NUMBER: 49:24179
ORIGINAL REFERENCE NO.: 49:4725i,4726a-d
TITLE: Pyridyl aliphatic amines. Antihistamines
PATENT ASSIGNEE(S): Schering Corp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 699852		19531118	GB	

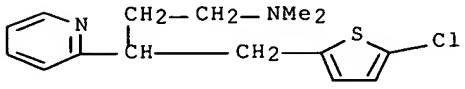
AB To KNH2 1.0 mole in liquid NH3 3 l. is added 2-benzylpyridine 1.0 mole. After 15 min. β-dimethylaminoethyl chloride is added, the NH3 evaporated, H2O added, the mixture extracted with Et2O, the Et2O evaporated, and the residue distilled, giving 3-phenyl-3-(2-pyridyl)-N,N-dimethylpropylamine, b1-2 139-42°. To KNH2 1.0 mole in 3 l. liquid NH3, is added α-picoline 1.0 mole and after 15 min., 2-thienylmethyl chloride 1.0 mole. The NH3 evaporated, H2O added, the H2O layer extracted with Et2O, back-extracted with dilute HCl, the HCl layer made alkaline with NH4OH, extracted with Et2O, the Et2O extract dried over anhydrous Na2SO4, and the residue distilled gave 1-(2-pyridyl)-2-(2-thienyl)ethane (I), b0.5 106-10°, nD24 1.5780. I brominated in AcOH, NH3 added, the mixture extracted with Et2O, the extract dried and concentrated gave 1-(5-bromo-2-thienyl)-2-(2-pyridyl)ethane (II), b0.5 129-33°, nD26 1.6039. II (1.0 mole) is added to 1.0 mole KNH2 in 3 l. of liquid NH3, 1.1

mole of β-dimethylaminoethyl chloride added after 15 min., NH3 evaporated, H2O added, and the mixture extracted with Et2O to give 4-(5-bromo-2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.5 145-8°. In a similar manner 4-(5-chloro-2-thienyl)-3-(2-pyridyl)- N,N-dimethylbutylamine, b0.5 140-4°, can be obtained. Under N to 1 mole of 2-hexylpyridine in Et2O is added 1.0 mole of BuLi in anhydrous Et2O. After refluxing for several hrs., 1.1 mole of β-dimethylaminoethyl chloride in Et2O is added, the mixture refluxed 6 hrs., H2O added, Et2O layer separated, dried over anhydrous Na2SO4, and Et2O distilled, giving 3-(2-pyridyl)-N,N-dimethyloctylamine (III), b1.5 104-105°, nD31 1.4840; HCl salt, m. 117-19°; tartrate, m. 114-15°; mono-H succinate, m. 99.5-100° (from pentanol); mono-H maleate, m. 106-7° (from pentanol).

IT *717922-20-8P*, Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- *873407-08-0P*, Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]-
RL: PREP (Preparation)
(preparation of)

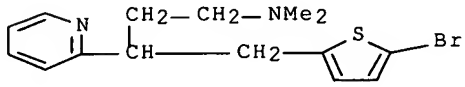
RN 717922-20-8 CAPLUS

CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



RN 873407-08-0 CAPLUS

CN Pyridine, 2-[1-(5-bromo-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1954:36070 CAPLUS
DOCUMENT NUMBER: 48:36070
ORIGINAL REFERENCE NO.: 48:6472a-g
TITLE: Antihistaminic substances
INVENTOR(S): Sperber, Nathan; Papa, Domenick; Schwenk, Erwin
PATENT ASSIGNEE(S): Schering Corp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 690274		19530415	GB 1948-27020	19481018

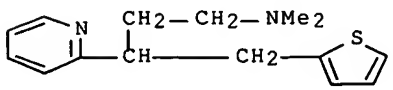
AB Antihistaminic substances of the general formula PyCHR'YR, where Y is an alkylene group having 2 or 3 C atoms, Py is a pyridine ring which may be substituted by a halogen, alkoxy, or lower alkyl group, R is a dialkylamino,

piperidino, morpholino, or imidazolinyl group, and R' is an alkyl, aryl, aralkyl, cycloalkyl, or heterocyclic group or an alkyl, alkoxy, dialkylamino, Cl, or Br derivative of such groups, and the inorg. and organic acid salts of the above-mentioned substances possess to an extremely high degree antihistaminic and antianaphylactic activity. Clin. studies have demonstrated comparative absence of any sedation, dizziness, or depression in 85-90% of the cases treated. The products are formed by the hydrolysis and decarboxylation (with a strong acid) of the nitriles of the general formula PyCR'(YR)CN. In an example, α-phenyl-α-(2- dimethylaminoethyl)-2-pyridineacetonitrile 400 is added to 80% H_2SO_4 2000 g., the mixture heated with stirring 24 h. at 140-50°, diluted with ice and water, the aqueous solution made alkaline with NH_3 gas, the oil which seps. extracted with ether, the extract dried, the ether removed, and the residue distilled, yielding 3-phenyl-3-(2-pyridyl)-N,N-dimethylpropylamine, b1-2 139-42°. The following compds., having substantial antihistaminic activity, may be prepared similarly: 3-phenyl-3-(2-pyridyl)-N,N- diethylpropylamine, a yellow oil, b1 156°, from α-phenyl-α-(2-diethylaminoethyl)-2-pyridineacetonitrile; 4-phenyl-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.5 135°, from α-benzyl-α-(2-dimethylaminoethyl)-2-pyridineacetonitrile; 3-(2-thienyl)-3-(2-pyridyl)-N,N-dimethylpropylamine, a pale yellow oil, b2 154°, from α-(2-thienyl)-α-(2-dimethylaminoethyl)-2-pyridineacetonitrile; 4-(2-thienyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, b0.1 130-3°, from α-(2-thienylmethyl)-α-(2- dimethylaminoethyl)-2-pyridineacetonitrile; 3-(p-tolyl)-3-(2-pyridyl)-N,N- dimethylpropylamine, b0.5 130-5°, from α-(p-tolyl)-α-(2- dimethylaminoethyl)-2-pyridineacetonitrile; 3-(p-methoxyphenyl-3-(2- pyridyl)-N,N-dimethylpropylamine, b0.5 137-42°, from α-(p-methoxyphenyl)-α-(2-dimethylaminoethyl)-2- pyridineacetonitrile; 3-(p-isopropylphenyl)-3-(2-pyridyl)-N,N- dimethylpropylamine, b1 144-7°, from α-(p-isopropylphenyl)- α-(2-dimethylaminoethyl)-2-pyridineacetonitrile; 3-phenyl-3-(6-methyl-2-pyridyl)-N,N-dimethylpropylamine, b1 171-5°, from α-(2-dimethylaminoethyl)-α-(6-methyl-2- pyridyl)phenylacetonitrile; 3-(p-bromophenyl)-3-(2-pyridyl)-N,N- dimethylpropylamine, b0.5 147-52°, from α-(p-bromophenyl)- α-(2-dimethylaminoethyl)-2-pyridineacetonitrile; 4-phenyl-4-(2-pyridyl)-2-dimethylaminobutane, from α-phenyl-α- (2-pyridyl)-γ-dimethylaminovaleronitrile; 4-phenyl-4-(2-pyridyl)-N,N- dimethylbutylamine, from α-phenyl-α-(2-pyridyl)-γ- (dimethylaminomethyl)butyronitrile; 3-phenyl-2-(2-pyridyl)-N,N- dimethylpropylamine, from α-benzyl-α-(2-pyridyl)-β-dimethylaminopropionitrile; 3-cyclohexyl-3-(2-pyridyl)-N,N-dimethylpropylamine, from α-cyclohexyl-α-(2- dimethylaminoethyl)-2-pyridineacetonitrile; 3-cyclohexyl-4-(2-pyridyl)-N,N- dimethylbutylamine, from β-cyclohexyl-α-(2-dimethylaminoethyl)- α-(2-pyridyl)propionitrile; 3-(5-bromo-2-thienyl)-3-(2-pyridyl)-N,N- dimethylpropylamine, from α-(5-bromo-2-thienyl)-α-(2- dimethylaminoethyl)-2-pyridineacetonitrile; 4-(p-bromophenyl)-3-(2-pyridyl)-N,N-dimethylbutylamine, from α-(p-bromobenzyl)-α-(2-dimethylaminoethyl)-2-pyridineacetonitrile.

IT ***672304-71-1P***, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]-
RL: PREP (Preparation)
(preparation of)

RN 672304-71-1 CAPLUS

CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



L58 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1953:3335 CAPLUS Full-text
DOCUMENT NUMBER: 47:3335
ORIGINAL REFERENCE NO.: 47:575i,576a-i,577a-i,578a-i,579a-h
TITLE: Histamine antagonists. γ,γ-Disubstituted N,N-dialkyl-propylamines
AUTHOR(S): Sperber, Nathan; Papa, Domenick; Schwenk, Erwin; Sherlock, Margaret; Fricano, Rosemarie
CORPORATE SOURCE: Schering Corp., Bloomfield, NJ
SOURCE: Journal of the American Chemical Society (1951), 73, 5752-9
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C.A. 45,9542c. Dialkylaminoalkanes were synthesized by various methods and tested as histamine antagonists. 3-Phenyl-3-(2-pyridyl)-N,N-dimethylpropylamine (I) and 3-(p-chlorophenyl)-3-(2-pyridyl)-N,N-dimethylpropylamine (II) were effective clinically. In general the most active compds. were derivs. of N,N-dimethylpropylamine with a 2-pyridyl and a Ph, p-substituted Ph, or heterocyclic group in the 3-position. 3-Pyridylacetamide (III) (25 g.) and 31 g. P2O5 heated to 360° at 15-20 mm. and the oil which distilled over at 145-210° redistd. yielded 9 g. 3-pyridineacetonitrile (IV), b1.5 101-9°, nD31 1.5216. III (45 g.), 30 g. NaCl, and 300 cc. (CH2Cl)2 stirred 15 min., 26 cc. POCl3 added, the mixture refluxed 9 hrs., and decomposed with dilute NaOH yielded 26.5 g. IV, b1 92-100°, nD31 1.5249. The method used for IV yielded 71.5% 2-pyridineacetonitrile (V), b0.5 80-5°, nD29 1.5193; with P2O5 the yield of V was 12%, b2 96-101°, nD30 1.5201. 2-Aminopyrimidine (19 g.) in 100 cc. concentrated HCl at -10° treated during 1 hr. with 25 g. NaNO2 in 40 cc. water, the mixture let warm to 0°, made basic with dry NH3, and cooled yielded 12 g. 2-chloropyrimidine, m. 65-6° (from C6H6-petr. ether). Method A: p-ClC6H4CH2CN was alkylated with Me2NCH2CH2Cl, the mixture extracted with 15% HCl, the acid exts. made basic with NH3, the oil extracted with Et2O, the Et2O evaporated, and the residue distilled in vacuo; α-(2-dimethylaminoethyl)-p- chloro-phenylacetonitrile (56 g.) and 41 g. 2-bromopyridine in 300 cc. PhMe treated with the NaNH2 from 6.5 g. Na in 100 cc. PhMe, the mixture refluxed 4 hrs., cooled, decomposed with water, the aqueous layer extracted with C6H6, and the combined C6H6-PhMe solns. distilled in vacuo yielded α-(p-chlorophenyl)-α-(2-dimethylaminoethyl)-2-pyridineacetonitrile. Method B: PhCH2CN with 2-Cl or 2-bromopyridine and 2 moles NaNH2 yielded α-phenyl-2-pyridineacetonitrile (VI); VI (87.6 g.) and 69 g. Me2NCH2CH2Cl in 300 cc. PhMe treated slowly with the NaNH2 from 11.3 g. Na in 300 cc. PhMe, the mixture refluxed 2 hrs., cooled, decomposed with water, and the PhMe layer distilled in vacuo yielded α-phenyl-α-(2-dimethylamino-ethyl)-2-pyridineacetonitrile (VH). Method C: VII (100 g.) added slowly to 400 g. cooled 75% H2SO4 the mixture heated approx. 1 hr. at 130-40°, the heating continued 6-10 hrs. (until no more CO2 was evolved), and the mixture poured on ice, made basic with NH3, and extracted with Et2O, yielded I. Method C1: NaNH2 (4.6 g. Na) in 75 cc. cold xylene treated with 31.5 g. α-(1-naphthyl)- α-(2-dimethylaminoethyl)-2-pyridineacetonitrile, the mixture refluxed 28 hrs., cooled, decomposed with water, and the xylene layer distilled in vacuo yielded 60% 3-(1-naphthyl)-3-(2-pyridyl)-N,N-dimethylpropylamine. EtLi (from 31 g. EtBr and 4.14 g. Li shot) in 100 cc. Et2O treated dropwise with 26.5 g. VII, the mixture stirred 4 hrs. at room temperature, decomposed with ice and dilute HCl, and the acid layer made alkaline with NH3 and extracted with Et2O yielded 15 g. I, b5 152-6°, nD21

1.5463. The EtMgBr from 6 g. Mg in 100 cc. PhOMe treated dropwise with 53.5 g. VII in 100 cc. PhOMe at 50-60°, the solution stirred 2 hrs. at 60-70°, cooled, decomposed with ice and dilute HCl, the organic layer extracted with dilute HCl, the exts. made alkaline with NH3, and the oil extracted with Et2O yielded 17 g. I, b3 149-52°, and 23 g. VII, b2 149-65°. Method D: KNH2 (27 g. K) in 2 l. NH3 treated with 115 g. 2-(p-methylbenzyl)pyridine, after 10 min. 75 g. Me2NCH2CH2Cl then 1 l. Et2O added, the mixture stirred 20 hrs. at room temperature, decomposed with water, and the Et2O layer fractionated yielded 3-(p-methylphenyl)-3-(2-pyridyl)-N,N-dimethylpropylamine. When NaNH2 was used the yield was 34%. Method D1: α-Dihydrostilbazole (36.6 g.) added slowly to BuLi (from 3.1 g. Li, 18.5 g. BuCl, and 120 cc. Et2O) at 0-10°, the mixture refluxed 1 hr., treated dropwise with 22 g. Me2NCH2CH2Cl, and stirred 18 hrs. yielded 4-phenyl-3-(2-pyridyl)-N,N- dimethylbutylamine. Method E: KNH2 (39 g. K) in 1.5 l. NH3 treated dropwise with 104 g. 2-picoline, the mixture stirred 20 min., 107.5 g. Me2NCH2CH2Cl added slowly, the solution stirred 11 hrs., the NH3 evaporated, the residue decomposed with saturated K2CO3, and the oil extracted with C6H6 yielded 111 g. 3-(2-pyridyl)-N,N-dimethyl-propylamine (VIII), b10 105-7°, nD28 1.4968. KNH2 (6.2 g. K) in 500 cc. NH3 treated with 25 g. VIII, the mixture stirred 15 min., 22 g. 2-chlorothiazole added, then 300 cc. Et2O, the mixture stirred 4 hrs., and decomposed with water yielded 3-(2-pyridyl)-3-(2- thiazolyl)-N,N-dimethylpropylamine. KNH2 (4.2 g. K) in 500 cc. NH3 treated with 24 g. I in 250 cc. Et2O, the mixture stirred 30 min., 15 g. EtBr in 50 cc. Et2O added, the mixture stirred until the NH3 had evaporated, and decomposed with Et2O yielded 23 g. 3-(phenyl)-3-(2-pyridyl)-N,N- dimethylamine, b1.5 152-5°, m. 53-4°. , ,Table I; , ,Nitriles: R1R2R3CCN; , , , , Yield; R1, R2, R3, Method, (%), B.p./mm.; o-ClC6H4, H, CH2CH2NMe2, A, 58, 140-2/2.0; p-ClC6H4, H, CH2CH2NMe2, A, 66, 139-40/2.5; p-MeC6H4, H, CH2CH2NMe2, A, 79, 124-5/3.0; PhCH2, H, CH2NMe2, B, 54, 110-15/0.5; PhCH2, H, CH2CH2NMe2, A, 31, 115-20/0.5; 1-C10H7, H, CH2CH2NMe2, A, 75, 171-3/2.0; C6H11, H, CH2CH2NMe2, A, 59, 103-6/0.5; 2-C4H3S, H, CH2CH2NMe2, A, 42, 116-19/3.5; 2-C4H3SMe, H, CH2NMe2, B, 31, 110-15/0.5; 2-C5H4N, H, CH2CH2NMe2, B, 48, 108-12/0.5; 3-C5H4N, H, CH2CH2NMe2, A, 40, 112-16/1.0; o-ClC6H4, 2-C5H4N, H, B, 42, 165-70/2.0; p-ClC6H4, 2-C5H4N, H, B, 73, 163-7/2.5 (a); Ph, 3-Me-2-C5H3N, H, B, 68, 162-70/0.5 (b); Ph, 2-C5H4N, CH2CH2NMe2, A (B), 78 (74), 162-5/0.5 (c); Ph, 2-C5H4N, CH2CH2NEt2, B, 92, 162-4/0.3; Ph, 2-C5H4N, (CH2)3NMe2, B, 82, 168-70/1.0; Ph, 2-C5H4N, CH2CH(Me)NMe2, A, 63, 179-84/3.5; Ph, 2-C5H4N, MeCHCH2NMe2, A, 48, 159-65/0.5; Ph, 2-C5H4N, CH2CH2NC5H10, B, 89, 175-80/1.0; p-MeC6H4, 2-C5H4N, CH2CH2NMe2, A, 44, 172-4/1.0; p-MeOC6H4, 2-C5H4N, CH2CH2NMe2, A, 80, 180-5/1.0; o-ClC6H4, 2-C5H4N, CH2CH2NMe2, B, 33, 195-202/2.0; p-ClC6H4, 2-C5H4N, CH2CH2NMe2, A, 67, 183-8/3.0; Ph, 6-Me-2-C5H4N, CH2CH2NMe2, A, 74, 173-8/2.5; Ph, 4-C5H4N, CH2CH2NMe2, A, 76, 166-9/1.0; PhCH2, 2-C5H4N, CH2NMe2, B, 46, 147-52/0.5; PhCH2, 2-C5H4N, CH2CH2NMe2, A, 41, 150-5/0.5; 1-C10H7, 2-C5H4N, CH2CH2NMe2, A, 76, 205-20/1.5; C6H11, 2-C5H4N, CH2CH2NMe2, A, 50, 158-63/1.5; 2-C5H4N, 2-C5H4N, CH2CH2NMe2, B, 78, 167-73/0.5; 2-C5H4N, 3-C5H4N, CH2CH2NMe2, A, 35, 172-80/1.0; 2-C4H3S, 2-C5H4N, CH2CH2NMe2, A, 36, 150-8/1.0; Ph, 2-C3H2NS, CH2CH2NMe2, A, 83, 153-9/1.5; 2-C3H2NS, 2-C3H2NS, CH2CH2NMe2, B, 33, 162-8/1.0; C6H11, Ph, CH2CH2NMe2, A, 82, 156-60/1.5; (a) m. 68-9° (from C6H6-petr. ether); (b) m. 119-20° (from C6H6-petr. ether); (c) picrate, m. 147-7.5°. , , Table II; , , Compds. of the formula R1-CHR3-R2; , , , , Yield; R1, R2, R3, Method, (%), B.p./mm.; 2-C5H4N, Ph, CH2CH2NMe2, C (D), 88 (80), 127-9/1.0 (a); 2-C5H4N, Ph, CH2CH2NEt2, C, 85, 156-7/1.0; 2-C5H4N, Ph, (CH2)3NMe2, C, 89, 148-50/2.0; 2-C5H4N, Ph, MeCHCH2NMe2, C, 66, 155-6/3.0 (b); 2-C5H4N, Ph, CH2CH2NC5H10, C, 68, 176-7/3.5; 2-C5H4N, p-MeC6H4, CH2CH2NMe2, C (D), 50 (76), 152-4/3.0; 2-C5H4N, p-iso-PrC6H4, CH2CH2NMe2, D, 80, 149-51/1.0;, 2-C5H4N, p-MeOC6H4, CH2CH2NMe2, D, 79, 172-5/1.5; 2-C5H4N, p-HOC6H4, CH2CH2NMe2, .., 21, 210-12/2.0 (c); 2-C5H4N, o-ClC6H4, CH2CH2NMe, C (D), 63 (75), 155-7/1.0; 2-C5H4N, p-ClC6H4, CH2CH2NMe2, C (D), 85 (82), 141-3/1.0 (e); 2-C5H4N, p-ClC6H4, CH2CH2NEt2, D, 73, 159-61/0.5; 2-C5H4N, 3,4-Cl2C6H3, CH2CH2NMe2, D, 53, 168-75/1.5; 2-C5H4N, p-Me2NC6H4, CH2CH2NMe2, D, 75, 178-83/1.5;, 2-C5H4N, PhCH2, CH2CH2NMe2, C (D),

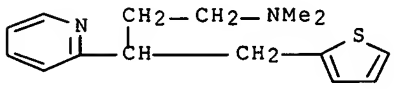
55 (83), 136-8/1.5 (f); 2-C5H4N, p-MeC6H4CH2 CH2CH2NMe2, D1, 41, 137-40/1.0 (g); 2-C5H4N, p-MeOC6H4CH2, CH2CH2NMe2, D, 82, 172-5/0.5 (h); 2-C5H4N, p-HOC6H4CH2, CH2CH2NMe2, .., 40, 215-30/3.0 (c); 2-C5H4N, 1-C10H7, CH2CH2NMe2, C1, 68, 183-6/1.0; 2-C5H4N, C6H11, CH2CH2NMe2, D, 38, 147-9/4.0; 2-C5H4N, Bu, CH2CH2NMe2, D, 89, 91-5/1.0; 6-Me-2-C5H3N, Ph, CH2CH2NMe2, C, 72, 137-9/1.0; 3-Me-2-C5H3N, Ph, CH2CH2NMe2, D, 50, 122-7/0.5; 4-C5H4N, Ph, CH2CH2NMe2, C, 82, 150-1/1.0; 4-C5H4N, PhCH2, CH2CH2NMe2, D, 27, 142-7/0.5; 2-C4H3N2, Ph, CH2CH2NMe2, C, 20, 127-30/0.5; 2-C3H2NS, Ph, CH2CH2NMe2, C, 92, 124-6/1.0; 2-C5H4N, 2-C5H4N, CH2CH2NMe2, C, 91, 145-50/1.0; 2-C5H4N, 3-C5H4N, CH2CH2NMe, C, 79, 131-6/1.0; 2-C5H4N, 2-C4H3S, CH2CH2NMe2, C, 30, 125-8/1.0; 2-C5H4N, 2-C4H3SCH, CH2CH2NMe2, D, 66, 168-70/3.0; 2-C5H4N, 5-ClC4H2SCH, CH2CH2NMe2, E, 55, 160-3/2.0; 2-C5H4N, 2-C5H4NS, CH2CH2NMe2, E, 24, 138-41/1.5; (a) dipicrate, m. 203-4°; oxalate, m. 152-2.5°; maleate, m. 107-8°. (b) R3 is mixture of isomers. (c) dipicrate, m. 199-200°. (e) maleate, m. 132.5-33°. (f) dipicrate, m. 204-5°. (g) dipicrate, m. 186-7°. (h) dipicrate, m. 167-8°. Li shot (4.2 g.) in 200 cc. Et2O under N treated dropwise with 41 g. BuBr at -10°, the mixture stirred 1 hr., cooled to -40°, 47.4 g. 2-bromopyridine added dropwise, the mixture stirred 30 min., 53 g. BzCH2CH2NMe2 added dropwise, the mixture stirred several hrs. at room temperature, decomposed with ice and dilute HCl, the aqueous layer made basic with NH3, and extracted with Et2O yielded 38 g. 1-phenyl-1-(2-pyridyl)-3-dimethylamino-1- propanol, (IX), b1.5 145-50°, m. 101-2° (from petr. ether). IX (20 g.) in 100 cc. 80% H2SO4 stirred 10 min. at 160°, the mixture poured on ice, made alkaline with cold, dilute NaOH, and extracted with Et2O yielded 15 g. 1-phenyl-1-(2-pyridyl)-3-dimethylamino-1-propene (X), b1.0 138-40°. X (5 g.) in 100 cc. AcOH shaken 30 min. with 2.5 g. 5% Pd-on-C at 60 lb./sq. in. pressure H, the filtrate concentrated in vacuo, the residue treated with 100 cc. 10% NaOH, the oil extracted with Et2O, the Et2O evaporated, and the residue treated with picric acid yielded the dipicrate of I, m. 199-200°. 2-Bromopyridine (158 g.) and 98 g. Me2NCH2CH2CN in 400 cc. refluxing PhMe treated with the NaNH2 from 26 g. Na in 300 cc. PhMe, the mixture refluxed 4 hrs., cooled, decomposed with water, the organic layer separated from the tar, the PhMe removed in vacuo, and the residue fractionated yielded 13 g. α-2-pyridylpyridine, b3.5-4 171-85°, m. 138-9° (from C6H6-petr. ether). Me2N(CH2)3CN (XI) (28 g.) and 40 g. 2-bromopyridine in 200 cc. PhMe at 60° treated with the NaNH2 from 12 g. Na in 250 cc. PhMe, the mixture stirred 6 hrs., decomposed with water, and the product distilled yielded 10.2 g. 3,3-bis(2-pyridyl)-N,N-dimethylpropylamine, b2 145-50°. XI (22.4 g.) and 51 g. 2-chlorothiazole in 150 cc. PhMe treated dropwise with the NaNH2 from 8 g. Na in 150 cc. PhMe, the mixture refluxed 4 hrs., cooled, and decomposed with water yielded α,α-bis(2-thiazolyl)-α-(dimethylamino)butyronitrile. MeNCH2CH2CN (25 g.) in 100 cc. PhMe at 85° treated dropwise with a mixture of the NaNH2 from 6.2 g. Na and 32.2 g. PhCH2Cl in 200 cc. PhMe, the mixture refluxed 7 hrs., cooled, decomposed with water, the aqueous layer extracted with C6H6, the combined C6H6-PhMe layers extracted with 10% HCl, and the acid exts. made basic with NH3 yielded α-dimethylaminoethyl-β-phenylpropionitrile (XII); the NaNH2 from 200 cc. xylene treated with 20 g. XII, then with 20 g. 2-bromopyridine (cautiously), the mixture refluxed 8 hrs., cooled, and decomposed yielded α-dimethylaminoethyl-α-benzyl-2- pyridineacetonitrile (XIII); 80% H2SO4 at 140-50° did not hydrolyze or decarboxylate XIII. I (24 g.) in MeOH reduced 4 hrs. with Raney Ni at 1.000 lb./sq. in. initial H pressure and 170°, the filtrate and washings concentrated in vacuo, and the residue distilled yielded 8.2 g. Fraction A, b1 105-21°, nD29 1.5292; and 12 g. Fraction B, b1 126-32°, nD30 1.5196; B on redistn. yielded γ-phenyl-γ- (N-methyl-2-piperidyl)-N,N-dimethylpropylamine (XIV), b0.5 122-5°, nD30 1.5193; picrate, m. 200-4°. A on redistn. b0.5 100-105°, nD30 1.5299; apparently the Me2N group has been lost. I (24 g.) in 190 cc. absolute EtOH treated as rapidly as possible with 27.4 g. Na, 90 cc. EtOH added, the mixture refluxed on the steam bath until the Na dissolved, concentrated in vacuo, the residue treated with water, and the oil extracted

with Et2O, the Et2O evaporated, and the residue distilled yielded 14.2 g. 3-phenyl-3-(2-piperidyl)-N,N-dimethylpropylamine (XV), b0.1 117-20°, nD28 1.5249. XV (8.5 g.) added dropwise to 6 cc. cooled 90% HCO2H, 6 cc. 37% formalin added, the mixture heated overnight on the steam bath, 20 cc. 10% HCl added, the solution concentrated in vacuo, and the residue made basic with NaOH and extracted with Et2O yielded 7 g. XIV, b1 127-34°, nD27 1.5231; picrate, m. 204-5°.

IT ***672304-71-1P***, Pyridine, 2-[3-dimethylamino-1-(2-thenyl)propyl]-
717922-20-8P, 2-Thiophenebutylamine, 5-chloro-N,N-dimethyl-γ-2-pyridyl-
RL: PREP (Preparation)
(preparation of)

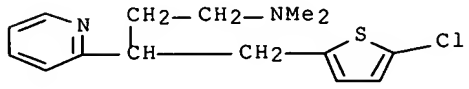
RN 672304-71-1 CAPLUS

CN 2-Thiophenebutylamine, N,N-dimethyl-γ-2-pyridyl- (5CI) (CA INDEX NAME)



RN 717922-20-8 CAPLUS

CN Pyridine, 2-[1-(5-chloro-2-thenyl)-3-dimethylaminopropyl]- (5CI) (CA INDEX NAME)



L58 ANSWER 15 OF 17 MARPAT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 139:271046 MARPAT Full-text

TITLE: Pharmaceutical compositions containing immunosuppressant thiophene amino alcohols and preparation of their intermediates

INVENTOR(S): Nishi, Takehide; Takemoto, Toshiyasu; Nara, Futoshi; Shimozato, Ryuichi

PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 150 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003267974	A	20030925	JP 2003-1715	20030108
PRIORITY APPLN. INFO.:			JP 2002-4425	20020111

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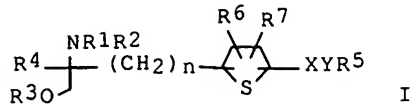
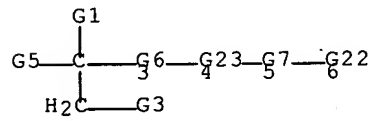


I

AB The compns., useful for prevention and treatment of autoimmune diseases, chronic articular rheumatism, and transplant rejection, contain amino alcs. I (R1-R3 = H, protective group; R4 = lower alkyl; n = 1-6; X = ethylene, vinylene, ethynylene, etc.; Y = single bond, C1-10 alkylene, etc.; R5 = H, cycloalkyl, aryl, heterocyclyl, etc.; R6, R7 = H, halo, lower alkyl, etc.), their salts, esters, or their derivs. (4R)-[2-[5-(5-cyclohexylpent-1-ynyl)thiophen-2-yl]]ethyl-4- methyloxazolidin-2-one (preparation given) was treated with KOH in THF/MeOH/H2O under reflux for 18 h to give 83% (2R)-amino-2-methyl-4-[5-(5- cyclohexylpent-1-ynyl)thiophen-2-yl]butan-1-ol, which showed host vs. graft reaction inhibition in rats with ID50 of 0.0843 mg/kg.

MSTR 1



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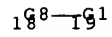
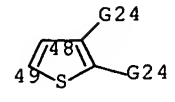


G8 = S
G12 = NH2
G13 = alkylene <containing 1-11 C>
(opt. substd. by (1-3) G12)
G22 = Ph (opt. substd. by (1-3) G30)
G23 = 49-3 48-5



G24 = CN
Patent location: claim 1
Note: or pharmacologically acceptable salts or esters

Note: additional heteroatom interruptions also claimed
Note: substitution is restricted

L58 ANSWER 16 OF 17 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 136:134664 MARPAT Full-text
TITLE: Preparation of aminoalkanol moiety-containing thiophene derivatives as immunosuppressants
INVENTOR(S): Nishi, Takahide; Takemoto, Toshiyasu; Shimozato, Takaichi; Nara, Futoshi
PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan
SOURCE: PCT Int. Appl., 373 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
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US 6964976	B2	20051115		

PRIORITY APPLN. INFO.:

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WO 2001-JP5988	20010710
US 2003-337702	20030107

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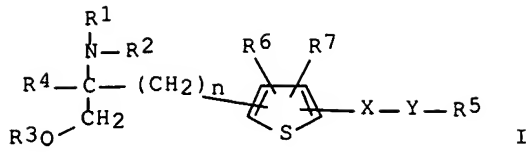

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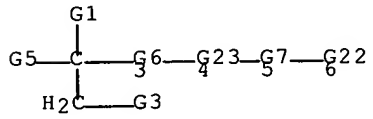
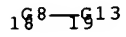
AB The title compds. I [R1 and R2 are each hydrogen or an amino-protecting group; R3 is hydrogen or a hydroxyl-protecting group; R4 is lower alkyl; n is an integer of 1 to 6; X is ethylene, etc.; Y is (un)substituted C1-10 alkylene, etc. ; R5 is aryl, etc.; and R6 and R7 are each hydrogen, alkyl, etc.; a proviso is given] are prepared Processes for preparing intermediates for I are claimed. (2R)-Amino-2-methyl-4-[5-[3-(4- methylphenoxy)propynyl]thiophen-2-yl]butan-1-ol maleic acid salt showed oral ID50 of 0.04 mg/kg against adjuvant arthritis in rats.

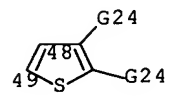
MSTR 1



G7 = 18-4 19-6



G8 = S
G12 = NH2
G13 = alkylene <containing 1-11 C>
(opt. substd. by (1-3) G12)
G22 = Ph (opt. substd. by (1-3) G30)
G23 = 49-3 48-5



G24 = CN
Patent location: claim 1
Note: or pharmacologically acceptable salts or esters
Note: additional heteroatom interruptions also claimed
Note: substitution is restricted

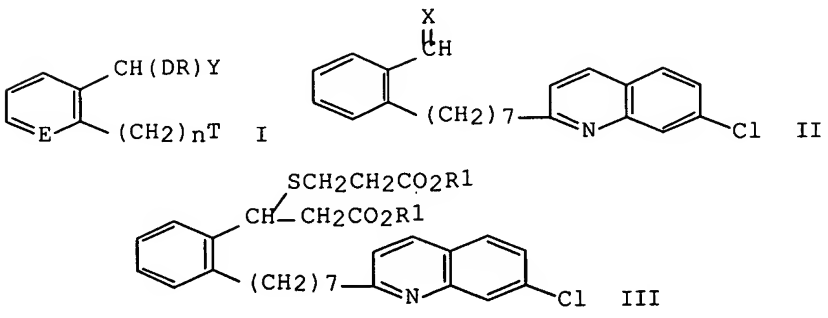
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 17 OF 17 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 115:71417 MARPAT Full-text
TITLE: Preparation and formulation quinolinyl-substituted propionic acid derivatives as leukotriene antagonists
INVENTOR(S): Cousins, Russell D.; Frazee, James S.; Gleason, John G.; Hall, Ralph F.
PATENT ASSIGNEE(S): SmithKline Beecham Corp., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

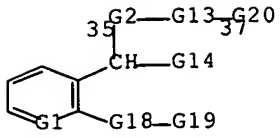
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4996214	A	19910226	US 1990-545258	19900628
CA 2083710	A1	19911229	CA 1991-2083710	19910614
WO 9200279	A1	19920109	WO 1991-US4262	19910614
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9182388	A	19920123	AU 1991-82388	19910614
EP 536310	A1	19930414	EP 1991-913413	19910614
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05508411	T	19931125	JP 1991-512612	19910614
ZA 9104959	A	19920624	ZA 1991-4959	19910627
PRIORITY APPLN. INFO.:			US 1990-545258	19900628
			WO 1991-US4262	19910614

GI

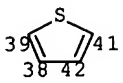


AB The title compds. [I; E = CH, N; D = O, SOq (wherein q = 0-2); R = (CH2)mA (wherein A = heterocyclyl, (substituted) Ph, etc.; m = 1-4); Y = tetrazolyl, CO2H or its ester or salt, (substituted) carbamoyl, etc.; T = haloquinolyl; n = 4-11] are prepared Wittig reaction of benzaldehyde derivative II (X = O) with Ph3P:CHCO2Me in MePh under Ar gave cinnamate II (X = CHCO2Me), which was treated with HSCH2CH2CO2Me and Et3N in MeOH at room temperature to give diester III (R1 = Me) (IV). Hydrolysis of diester IV with HCl in MeCN gave diacid III (R1 = H), which showed LTD4 antagonist activity with a Ki of 7.7 nmol. Inhalant, tablet, and suppository formulations were also given.

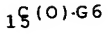
MSTR 1E



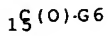
G1 = CH
G2 = S
G6 = NH2
G13 = 39-35 38-37 / 39-35 42-37 / 39-35 41-37 /
38-35 39-37 / 38-35 42-37 / 38-35 41-37



G14 = 15

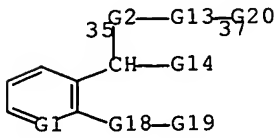


G20 = 15 / CN



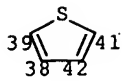
Derivative: or pharmaceutically acceptable salts
Patent location: claim 1

MSTR 2F



G1 = CH
G2 = S

G6 = NH2
G13 = 39-35 38-37 / 39-35 42-37 / 39-35 41-37 /
38-35 39-37 / 38-35 42-37 / 38-35 41-37



G14 = 15

$_{15}C(O)\text{-}G6$

G20 = 15 / CN

$_{15}C(O)\text{-}G6$

Derivative: or pharmaceutically acceptable salts
Patent location: disclosure

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=> d his full

     (FILE 'HOME' ENTERED AT 08:08:37 ON 20 FEB 2007)

     FILE 'REGISTRY' ENTERED AT 08:08:52 ON 20 FEB 2007

     FILE 'CAPLUS' ENTERED AT 08:09:14 ON 20 FEB 2007
               ACT LAM728APP/A
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L1             1 SEA ABB=ON  PLU=ON  US2005-521728  /AP
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     FILE 'REGISTRY' ENTERED AT 08:09:33 ON 20 FEB 2007
               ACT LAM728RNS/A
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L2            10 SEA ABB=ON  PLU=ON  (125978-95-2/BI OR 2549-14-6/BI OR
                 329900-75-6/BI OR 36155-82-5/BI OR 496836-30-7/BI OR 651034-24-
                 1/BI OR 651034-29-6/BI OR 651034-45-6/BI OR 86013-50-5/BI OR
                 98-91-9/BI)
              ---------
               ACT LAM728L9L12/A
              ---------
L3               STR
L4               STR
L5          2142 SEA SSS FUL L3 AND L4
              ---------

     FILE 'CAPLUS' ENTERED AT 08:10:11 ON 20 FEB 2007
L6           450 SEA ABB=ON  PLU=ON  L5

     FILE 'REGISTRY' ENTERED AT 08:10:28 ON 20 FEB 2007
L7             2 SEA ABB=ON  PLU=ON  L5 AND L2
                 D SCA
L8             8 SEA ABB=ON  PLU=ON  L2 NOT L7
                 D SCA

     FILE 'CAPLUS' ENTERED AT 08:12:41 ON 20 FEB 2007
L9             1 SEA ABB=ON  PLU=ON  L7
                 D L3
                 D L4

     FILE 'STNGUIDE' ENTERED AT 08:13:21 ON 20 FEB 2007

     FILE 'REGISTRY' ENTERED AT 08:14:59 ON 20 FEB 2007

     FILE 'STNGUIDE' ENTERED AT 08:19:20 ON 20 FEB 2007

     FILE 'REGISTRY' ENTERED AT 08:41:32 ON 20 FEB 2007
L10              STRUCTURE UPLOADED
L11           50 SEA SUB=L5 SSS SAM L10

     FILE 'STNGUIDE' ENTERED AT 08:44:58 ON 20 FEB 2007

     FILE 'CAPLUS' ENTERED AT 08:47:35 ON 20 FEB 2007
L12            0 SEA ABB=ON  PLU=ON  L11

     FILE 'REGISTRY' ENTERED AT 08:47:48 ON 20 FEB 2007
L13              STRUCTURE UPLOADED
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L14             0 SEA SSS SAM L13
L15            50 SEA SUB=L5 SSS SAM L13

     FILE 'STNGUIDE' ENTERED AT 08:50:15 ON 20 FEB 2007

     FILE 'REGISTRY' ENTERED AT 08:52:04 ON 20 FEB 2007
L16                STRUCTURE UPLOADED
L17            50 SEA SUB=L5 SSS SAM L16
L18                STRUCTURE UPLOADED
L19            50 SEA SUB=L5 SSS SAM L18
L20                STRUCTURE UPLOADED
L21             8 SEA SUB=L5 SSS SAM L20
                   D SCA
L22                STRUCTURE UPLOADED
L23             5 SEA SUB=L5 SSS SAM L22
                   D SCA
L24           206 SEA SUB=L5 SSS FUL L22
                   SAVE TEMP L24 LAM728STR22L/A

     FILE 'CAPLUS' ENTERED AT 09:10:45 ON 20 FEB 2007
L25           443 SEA ABB=ON  PLU=ON  L24

     FILE 'REGISTRY' ENTERED AT 09:11:03 ON 20 FEB 2007

     FILE 'CAPLUS' ENTERED AT 09:15:21 ON 20 FEB 2007

     FILE 'REGISTRY' ENTERED AT 09:16:26 ON 20 FEB 2007
L26             1 SEA ABB=ON  PLU=ON  65899-73-2
                   D SCA
L27           205 SEA ABB=ON  PLU=ON  L24 NOT L26

     FILE 'CAPLUS' ENTERED AT 09:16:55 ON 20 FEB 2007
L28           172 SEA ABB=ON  PLU=ON  L27

     FILE 'REGISTRY' ENTERED AT 09:17:21 ON 20 FEB 2007
L29             1 SEA ABB=ON  PLU=ON  99592-32-2
                   D SCA
L30           204 SEA ABB=ON  PLU=ON  L27 NOT L29

     FILE 'CAPLUS' ENTERED AT 09:17:53 ON 20 FEB 2007
L31            97 SEA ABB=ON  PLU=ON  L30
L32                ANALYZE PLU=ON  L31 1- RN :    9106 TERMS
                   D

     FILE 'REGISTRY' ENTERED AT 09:19:14 ON 20 FEB 2007
L33             1 SEA ABB=ON  PLU=ON  65899-73-2
L34             1 SEA ABB=ON  PLU=ON  99592-39-9
                   D SCA L33
                   D SCA L34
L35           203 SEA ABB=ON  PLU=ON  L30 NOT (L33 OR L34)

     FILE 'CAPLUS' ENTERED AT 09:20:03 ON 20 FEB 2007
L36            81 SEA ABB=ON  PLU=ON  L35

     FILE 'REGISTRY' ENTERED AT 09:21:38 ON 20 FEB 2007
L37                STRUCTURE UPLOADED
L38             0 SEA SUB=L5 SSS SAM L37
L39            31 SEA SUB=L5 SSS FUL L37
L40             2 SEA ABB=ON  PLU=ON  L39 AND L2
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     FILE 'CAPLUS' ENTERED AT 09:23:54 ON 20 FEB 2007
L41            16 SEA ABB=ON  PLU=ON  L39

     FILE 'REGISTRY' ENTERED AT 09:24:44 ON 20 FEB 2007
                D COST
                D SCA L40

     FILE 'STNGUIDE' ENTERED AT 09:34:12 ON 20 FEB 2007

     FILE 'REGISTRY' ENTERED AT 09:36:20 ON 20 FEB 2007
L42             STRUCTURE UPLOADED
L43           0 SEA SSS SAM L42
L44           2 SEA SSS FUL L42
                SAVE TEMP L44 LAM728STR42L/A
                D SCA

     FILE 'CAPLUS' ENTERED AT 09:38:23 ON 20 FEB 2007
L45           1 SEA ABB=ON  PLU=ON  L44

     FILE 'MARPAT' ENTERED AT 09:38:46 ON 20 FEB 2007
L46           0 SEA SSS SAM L42
L47          14 SEA SSS FUL L42
L48           4 SEA ABB=ON  PLU=ON  L47/COM
                D SCA
                D COST

     FILE 'CAPLUS' ENTERED AT 09:40:29 ON 20 FEB 2007
L49          39 SEA ABB=ON  PLU=ON  METE A?/AU
L50          49 SEA ABB=ON  PLU=ON  WALTERS I?/AU
L51           5 SEA ABB=ON  PLU=ON  L49 AND L50
L52           2 SEA ABB=ON  PLU=ON  (L41 OR L45) AND (L49 OR L50)

     FILE 'REGISTRY' ENTERED AT 09:42:23 ON 20 FEB 2007

     FILE 'CAPLUS' ENTERED AT 09:42:26 ON 20 FEB 2007
                D STAT QUE L51
                D STAT QUE L52
L53           6 SEA ABB=ON  PLU=ON  (L51 OR L52)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 09:43:21 ON 20 FEB 2007
L54           6 SEA ABB=ON  PLU=ON  L51

     FILE 'CAPLUS, MEDLINE, EMBASE, BIOSIS' ENTERED AT 09:43:38 ON 20 FEB 2007
L55           6 DUP REM L53 L54 (6 DUPLICATES REMOVED)
                    ANSWERS '1-6' FROM FILE CAPLUS
                D IBIB ABS HITSTR L55 1-6

     FILE 'REGISTRY' ENTERED AT 09:44:51 ON 20 FEB 2007

     FILE 'CAPLUS' ENTERED AT 09:44:54 ON 20 FEB 2007
                D STAT QUE L41
                D STAT QUE L45
L56          14 SEA ABB=ON  PLU=ON  (L41 OR L45) NOT L53

     FILE 'MARPAT' ENTERED AT 09:45:31 ON 20 FEB 2007
                D STAT QUE L48
L57           3 SEA ABB=ON  PLU=ON  L48 NOT L53

     FILE 'CAPLUS, MARPAT' ENTERED AT 09:46:10 ON 20 FEB 2007
L58          17 DUP REM L56 L57 (0 DUPLICATES REMOVED)
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ANSWERS '1-14' FROM FILE CAPLUS
ANSWERS '15-17' FROM FILE MARPAT
D IBIB ABS HITSTR L58 1-14
D IBIB ABS QHIT L58 15-17

FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6
DICTIONARY FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE CAPLUS

FILE COVERS 1907 - 20 Feb 2007 VOL 146 ISS 9
FILE LAST UPDATED: 19 Feb 2007 (20070219/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 16, 2007 (20070216/UP).

FILE MARPAT
FILE CONTENT: 1961-PRESENT VOL 146 ISS 7 (20070216/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

```
US   2007004775 04 JAN 2007
DE 102005029574 28 DEC 2006
EP      1739181 03 JAN 2007
JP   2006351418 28 DEC 2006
WO   2007004364 11 JAN 2007
GB      2427193 20 DEC 2006
FR      2887681 29 DEC 2006
RU      2290406 27 DEC 2006
CA      2510093 16 DEC 2006

Expanded G-group definition display now available.

FILE MEDLINE
 FILE LAST UPDATED: 17 Feb 2007 (20070217/UP).  FILE COVERS 1950 TO DATE.

  All regular MEDLINE updates from November 15 to December 16 have been
  added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
  and 2007 tree numbers.

  The annual reload will be available in early 2007.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

FILE EMBASE
 FILE COVERS 1974 TO 19 Feb 2007 (20070219/ED)

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 February 2007 (20070214/ED)

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